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BRITISH MEDICAL JOURNAL

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CLINICAL USES OF CURRENTLY AVAILABLE ANTIBIOTICS*

BY

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In approaching this subject I have taken the liberty of giving it a rather liberal interpretation. I have not considered it my task to present a thoroughly documented review of the clinical results that have been reported in the vast and rapidly growing literature on the medical uses of the currently available antibiotics. It has seemed to me more suitable to give some general views and interpretations concerning current clinical uses of available antibiotics, first from the point of view of the individual agents and then with respect to their application to special diseases or in special situations. There is still left too wide a range of topics, so that, of necessity, only a few can be touched upon, and these only briefly. For more complete reviews of recent literature with adequate documentation and interpretation the reader is referred to Dr. Welch's book, in its forthcoming revision, and to the papers in the *Annual Reviews of Microbiology* for the years 1951, 1952, and 1953 by Herrell, Kirby, and Heilman, respectively.

In recent years it has become abundantly clear that new antimicrobial agents with activity which clearly overlaps or even closely parallels that of previously available agents can achieve wide acceptance and use in a rather brief time. Moreover, new agents and some which had previously been unpopular, or generally thought to be inferior or even discarded, can gain acceptance and, in some instances, even supersede others which have been regarded as of proved efficacy or superiority. This phenomenon is of considerable significance in relation to the understanding of current usages and is open to diverse interpretations.

First and foremost, one is confronted with the fact that by far the greatest proportion of the antibiotics that are used to-day are prescribed for conditions which have no clear relation to the efficacy of those agents. Indeed, in most instances the relative efficacy of the various agents for the particular uses to which they are put has not been clearly assessed, and in fact is usually difficult or impossible to evaluate. In the choice of agents for most prophylactic purposes or for the treatment of mild and relatively unimportant infections, or for the combined use of multiple agents, preference is likely to be shown to those which are considered relatively harmless rather than to be superior. When any one agent is used freely over long periods and without proper indications, there almost inevitably comes an awareness of the sensitizing and other potential toxic effects of the agent so used and also of its inadequate therapeutic effectiveness. Under such circumstances it seems easier to shift to a new one rather than to become more selective with respect to the patients to be treated and agents to be used.

Investigators who conduct the initial clinical trials of new antibiotics in their anxiety to discover and reveal as much as possible about the potential usefulness of these agents often publish their results prematurely. Although they may present these results accurately and interpret the findings with the greatest caution, their findings and the conclusions are often grossly exaggerated and misinterpreted or given new meanings, both by readers who wish to justify some particular applications and by manufacturers who wish to exploit their products. Such preliminary trials can generally be expected to uncover only the broad outlines of the field of usefulness of a new agent. More definitive evaluations, concerning both the absolute and the relative efficacy and toxicity, require prolonged and controlled clinical trials, and such trials have only rarely been made before the use of a new and promising agent has already been widely adopted.

Real or apparent increases in clinical resistance have been encountered in infections caused by staphylococci, *Pseudomonas*, *Proteus*, and some coliform organisms (and possibly also enterococci and non-haemolytic streptococci); these have obviously offered a legitimate field for new antimicrobials or for changing the emphasis in the use of the available ones. Such changes, however, have frequently, and sometimes unavoidably, been carried beyond the proper and proved indications.

The desire of the physician to do everything possible and "not to miss a trick" has also led to the persistent use of agents in infections or conditions in which they are known to lack efficacy, such as viral, fungal, or parasitic diseases, and in fevers of undetermined aetiology, when an infectious agent cannot be readily determined or excluded. The fact that most of these patients recover in the course of such therapy seems to be accepted as adequate justification for continuing this practice.

Then there is the growing use of multiple agents. This has its legitimate origin and sanction from *in vitro* experiments with certain specific organisms and combinations of antibiotics, and also has been demonstrated in a very limited number of specific infections, likewise with well-defined combinations of antibiotics. It has, however, been broadened in general practice to include

*Based on a paper presented on October 28 at the Antibiotics Symposium held in Washington under the auspices of the Division of Antibiotics, Food and Drug Administration of the Department of Health, Education, and Welfare, in collaboration with the journal, *Antibiotics and Chemotherapy*, and reproduced by kind permission of Dr. Henry Welch, Director of the Division of Antibiotics.

†Aided by a grant from the United States Public Health Service.

almost all serious infections, or merely febrile illnesses that seem to resist treatment with individual agents. This use of combined therapy has reached the point where it is uncommon, in certain areas, to encounter a patient who has had fever for several days and has not already been given many agents, either in succession or, more often, simultaneously, so that he is receiving as many as four or even six antimicrobials at one and the same time. While most physicians are apt to be apologetic about such usage, others not only condone it but actually recommend it as the preferred practice.

Finally, there is the ever-present and overwhelming mass of commercial literature and persuasive advertising and "detailing" by manufacturers and their representatives, emphasizing the virtues of their own respective product and of course the glaring faults in the products of others, while ignoring or minimizing the limitations and undesirable features of their own products. This is an almost inevitable but also a very highly valuable feature of our free economy; but its advantages to the patient can be fully realized only if there is a properly critical attitude on the part of the physician at whom all this is directed.

Penicillin

It seems almost commonplace to mention that penicillin is still the most effective and least toxic agent available for the treatment of most infections due to organisms which are moderately or highly sensitive to it *in vitro*. Some of its usefulness, however, has been reduced by excessive and unnecessarily widespread usage over the past few years, which has resulted in the sensitization of large numbers of individuals and, in the case of the staphylococcus, by the gradual elimination of sensitive strains. The general recognition of the increase in resistance of pathogenic staphylococci to penicillin in all hospitals and communities where this agent is used very extensively has also raised the obvious question of whether penicillin might be losing some of its effectiveness in other infections for which it is generally employed. The tendency to prescribe dosages which appear inordinately high and ever increasing in relation to the previously known sensitivity of the strains of organisms in the diseases for which it is being used has inevitably given the impression of diminished efficacy; it is more likely, however, that this has little or no relation to any established factors other than fashion and usage.

Thus far, there appears to be no evidence of any decreased activity *in vitro* among recently isolated strains of organisms, at least of the more sensitive species—namely, gonococcus, pneumococcus, and group A streptococcus. Likewise, there seems to be no change in the clinical efficacy of penicillin against infections caused by these organisms. There also has been no significant change in the effectiveness of penicillin in the treatment of syphilis since the use of purified crystalline penicillin G was standardized. In subacute bacterial endocarditis, on the other hand, it is possible that some decrease in efficacy of penicillin is responsible for the present need for large doses. This, too, may have its origin in the widespread use of penicillin, which may have resulted in a general, though not so marked, reduction in the sensitivity of strains of the viridans group of streptococci, which are so universally present as part of the normal flora of the mouth and which are also the major cause of this disease.

Little can be said about the relative effectiveness of the various new forms of penicillin. L-Ephenamine penicillin G ("compenamine") and penicillin O (allylmercaptyl penicillin G), with its repository form chloroprocaine penicillin O, are presumed to be equivalent in their therapeutic effectiveness to penicillin G and to procaine penicillin; although this has not been conclusively proved, there is no evidence to the contrary. In the case of penethamate (the hydriodide of diethylaminoethyl ester of penicillin G, "neo-penil") conclusive proof is still lacking for any superiority in its therapeutic effectiveness over penicillin G or procaine penicillin in conditions in which a specific localization might be considered advantageous. These agents are of particular interest with respect to hypersensitivity reactions.

Perhaps the most important problem concerning penicillin relates to the choice of the dosage form for its systemic use. Oral penicillin in the buffered tablets of the sodium or potassium salts is well absorbed; even so, it is only about 10 to 30% efficient, so that from three to ten times the intramuscular dose is necessary to achieve the same therapeutic effect. Oral penicillin should therefore be entirely feasible for the therapy of infections with highly sensitive organisms such as gonococcus, group A streptococcus, or pneumococcus, and its relatively low sensitizing potential would tend to recommend it for such uses. However, experience with oral penicillin therapy of acute gonorrhoea, in which one is dealing with the most sensitive of these organisms, has not proved as satisfactory as with the intramuscular forms. Moreover, in sick patients suffering from severe infections in which large doses are required, it is often difficult to administer, and, in addition, may also entail gastro-intestinal disturbances similar to those encountered with other antibiotics (erythromycin, carbomycin, and the broad-spectrum antibiotics) when it is given in similar or larger total amounts. Oral penicillin cannot, therefore, be recommended as a dosage form of choice in the treatment of severe infections due to organisms which are only of low or moderate sensitivity to that antibiotic.

In approaching the problem of dosage and the choice of a parenteral form of penicillin for the treatment of infections with organisms that are only slightly or moderately sensitive, one must consider (1) the nature of the lesion, particularly with respect to the accessibility of the organisms within that lesion to penicillin reaching it from the circulating blood; (2) the density of the bacterial population at that site; and (3) the possibility of intervention of host or immune factors to aid in disposing of small numbers of residual organisms. For most of the background of our understanding of this subject we are indebted to the laborious and carefully designed studies of Eagle and his co-workers. He has established the rationale of large and intermittent dosage and the need for achieving concentrations in the blood which are many times the minimum *in vitro* inhibiting concentration, and also the necessity for long-continued treatment in order to eradicate established foci of infection in which there are large numbers of organisms. The experiments of Weinstein and his coworkers extended these findings and showed that if a sufficiently high concentration is achieved in the tissue fluids, effective concentrations can be reached within fibrin foci, and these concentrations will then drop more slowly than those of the surrounding tissue fluids.

From these observations, and from the very rapid rate of excretion of penicillin by the kidney, one may conclude that the intermittent intramuscular injection of the aqueous sodium or potassium salts is preferable to the repository preparation for the treatment of deep and walled-off foci of infection. Obviously, the longer the antibiotic remains in the repository site the flatter will be the curve of the concentrations within the blood and tissue fluids; also, the high gradient necessary to penetrate the walled-off foci is less readily achieved by such repository preparations. On the other hand, repository forms may be useful even for deep foci of infection, whenever the organisms are sufficiently sensitive and there is adequate access to tissue fluids, as may be the case in syphilitic or haemolytic streptococcal infections.

The same reasoning which has led to these conclusions also offers some rationale for the use of inhibitors of renal excretion of penicillin, such as probenecid ("benemid"), to raise the peak levels and sustain high concentrations between intermittent intramuscular injections; it could also be used as an argument for the support of the intermittent rapid intravenous injections as opposed to continuous intra-

venous injection during probenecid administration for the purpose of obtaining high peaks of concentrations in the treatment of subacute bacterial endocarditis or of walled-off foci of infection with organisms of low sensitivity.

Streptomycin

Although streptomycin remains the major mainstay in the treatment of tuberculosis, two important features have led to renewed interest in this agent and an increase in its systemic use in many non-tuberculous infections. One is the use of smaller doses (1 or 2 g. a day) and shorter courses, which minimize the occurrence of the major toxic effects of this antibiotic on the eighth nerve; the other is the use of streptomycin in combination with other agents, particularly with large doses of penicillin, which has resulted in an increase in its effectiveness against relatively resistant Gram-positive organisms, coupled with a reduction in the rate and degree of emergence of streptomycin-resistant variants. The latter usage is best typified in the treatment of bacterial endocarditis due to organisms which are only slightly sensitive to either penicillin or streptomycin separately. It is important, however, to avoid the use of streptomycin alone in such cases, lest resistant variants emerge rapidly during such use and subsequently interfere with the successful application of the combined therapy.

The rapid bactericidal action of streptomycin has, in our experience, been most helpful in the early acute stage of severe infections with Gram-negative bacilli, particularly in Friedländer's pneumonia, although the character of the necrotizing lesion in the latter has militated against its continued effectiveness and against its success in completely eliminating the organisms. Resort must then be had to other antibiotics to which the residual organisms are sensitive. Streptomycin is still useful either alone or together with other antimicrobial agents in the treatment of meningitis, infections of the urinary tract, and other severe infections with susceptible organisms; also, used together with penicillin and/or sulphonamides, it still has an important place in the prevention and treatment of generalized peritonitis. The importance of alkalinization of the urine in enhancing the effectiveness of streptomycin in the treatment of urinary tract infections cannot be overemphasized.

A serious question may be raised whether the generally prevailing use of dihydrostreptomycin in preference to streptomycin has a sound basis. It now seems clear that dihydrostreptomycin tends to produce a predominantly auditory-nerve damage which may be insidious and delayed in its onset and usually is irreversible; streptomycin, on the other hand, gives rise predominantly to vestibular dysfunction, which may be recognized early, and at that stage, if the treatment has stopped, may be reversible. Any difference in antimicrobial activity of the two agents *in vitro* or in experimental animals is probably slight, but it appears to be predominantly in favour of streptomycin, while no appreciable difference has been demonstrated in the clinical activity of these two forms. Is it not, therefore, more appropriate to consider streptomycin the first choice in therapy as between these two forms, with dihydrostreptomycin reserved for continuing the treatment when it is imperative to do so with evidence of sensitization, or possibly after symptoms of vestibular damage are first recognized? It is possible, however, that this problem may be resolved by the combined use of the two forms if present indications of the much lower toxicity of this combination are more firmly established.

The Tetracyclines

Now that the chemical kinship of "aureomycin" and "terramycin," which had long been suspected, has been fully established, it is appropriate to consider these two agents together and also to include the third one, tetracycline, which chemically has been divested of the distinguishing portions of the structure of each of the other two. Preliminary observations in our laboratory and clinic would point to a very close similarity in the antibacterial action of these three analogues *in vitro* and *in vivo*. The differences which have been noted *in vitro* seem to be related chiefly to the instability of aureomycin outside of the body, and the clinical differences appear to be related primarily to the lower toxicity of tetracycline.

The relative clinical efficacy of tetracycline may be extremely difficult to evaluate, just as we have found great difficulty in establishing any clear and overall differences in efficacy between aureomycin and terramycin. On the other hand, there seems little doubt that in isolated individual patients, there appears to be a gross and distinguishable difference in activity between the two latter agents, favouring the one or the other, and there may also prove to be such a difference in occasional patients or infections with respect to tetracycline and either or both of the other chemically related substances. From the point of view of toxicity, only the untoward gastro-intestinal effects lend themselves to comparison. Data thus far available would indicate that the use of tetracycline is accompanied by a significantly lower incidence of gastro-intestinal symptoms than is the use of aureomycin in comparable doses and in similar patients. Terramycin, in our clinic, has regularly produced an appreciably greater incidence of gastro-intestinal symptoms than aureomycin, particularly the diarrhoeas associated with displacement of the faecal flora by resistant staphylococci.

The tetracycline antibiotics are still highly effective against infections with a wide variety of Gram-positive and Gram-negative bacteria, including many types of bacterial meningitis. In our experience and in many other hospitals *intravenous* aureomycin has also proved to be the most effective single antimicrobial agent in the treatment of acute diffuse peritonitis. One interesting phenomenon that has been noted is the apparently striking efficacy of *intravenous* aureomycin in the treatment of peritonitis due to *Salmonella typhosa* and resulting from perforations of the bowel or of the gall-bladder complicating chloramphenicol-treated typhoid fever.

The tetracyclines are highly effective against all rickettsial infections, and they appear to be the most effective agents available against the psittacosis–lymphogranuloma–trachoma group of organisms. The effectiveness of all antibiotics against trachoma, however, has recently been questioned in some quarters. The popular misconception about the efficacy of these agents against "viruses" had led to many conflicting reports on their use in many diseases known or presumed to be of viral aetiology. In general, it is probably fair to state that no clear-cut proof of the effectiveness of these agents in uncomplicated viral infections has yet been brought forth. Moreover, although most workers have felt that the efficacy of aureomycin in the treatment of cases of primary atypical pneumonia of the type associated with cold agglutinins has been proved, some doubts have also been raised in this regard.

There is, however, clear evidence of a decreasing efficacy of aureomycin and terramycin in the treatment of some staphylococcal infections; this is associated with an increased incidence of staphylococci resistant to these agents. The decrease in effectiveness, however, seems to be limited primarily, or perhaps entirely, to nosocomial infections with staphylococci or to such infections acquired during the course of treatment with one of these agents, and they may in fact be confined to hospitals in which either or both of these agents have been very widely used. There is also a suggestion of a decrease in the effectiveness of the tetracyclines in the treatment of infections with some coliform organisms, particularly *Aerobacter aerogenes*.

Chloramphenicol

The clinical activity of this agent overlaps most of the range of infections which are favourably influenced by the tetracyclines. Chloramphenicol appears to be appreciably less effective against infections with Gram-positive organisms and probably also against the psittacosis–lymphogranuloma–trachoma group of infections. It is somewhat

more effective against some of the Gram-negative bacillus infections, particularly those due to salmonellae and many of the *Proteus* organisms. It is also about as effective as the tetracyclines in rickettsial infections. Chloramphenicol is highly effective in *Haemophilus influenzae* meningitis, and is considered by some authors to be the agent of choice in this disease.

Of prime interest is the fact that although chloramphenicol is generally much less active than penicillin and significantly less active than the tetracyclines against staphylococci *in vitro*, strains of moderate or high resistance to chloramphenicol are rarely encountered. As a result, chloramphenicol has recently proved to be highly useful in the treatment of serious infections due to staphylococci that are resistant to penicillin and to the tetracyclines.

In the treatment of salmonella infections, although chloramphenicol is generally considered to be the agent of choice, it must be conceded that this has been clearly demonstrated only with respect to the clinical response of patients with typhoid fever. Even in this disease, however, the efficacy of chloramphenicol leaves much to be desired, for the most frequent complications in this disease—namely, relapse, perforation, haemorrhage, cholecystitis, and the carrier state—are not entirely prevented; possibly some of them, particularly relapses, have not been reduced at all in frequency even by prolonged therapy with adequate or large doses. In other serious salmonella infections in humans, as in *Salmonella typhi-murium* infections in mice, there is to my knowledge little evidence of any striking and lasting therapeutic benefit from chloramphenicol.

One is hardly justified at this time in leaving the discussion of the clinical use of chloramphenicol without expressing some opinion concerning the severe and fatal bone-marrow depressions which have been attributed to this agent. Extreme views have been expressed on this subject; some have felt that the sale of the drug should be entirely prohibited, while others have even manifested serious doubts that chloramphenicol has been conclusively proved to be the cause of any of the cases of bone-marrow depression which have been attributed to it. Judging solely from the published data, however, it seems difficult to escape the conviction that at least a significant proportion of the cases of blood dyscrasias that have been described may reasonably be attributed to the use of this drug, but that, on the whole, this complication is rare considering the frequency with which chloramphenicol has been used. It also seems reasonable to recommend, as did the National Research Council's *ad hoc* committee, that this agent should not be used repeatedly for minor indications, for prophylaxis, or where any risk at all would be difficult to justify. On the other hand, in the treatment of those significant and serious infections for which chloramphenicol is clearly preferred or indicated on the basis of its known clinical performance, there seems no reason to hesitate to use it.

It has generally been recommended that frequent blood counts be made if chloramphenicol is to be used. Actually such counts, if done at frequent intervals during an initial course of treatment of the average duration, can hardly yield information of value, since by far the majority of cases of blood dyscrasias that may arise probably would show little change until some time after treatment is discontinued. It is possible, of course, that some appropriate test may be devised which would reveal the earliest evidence of such potential trouble, and haematologists should be encouraged in every way to attempt to find such a test. However, a rapid drop in the total leucocyte or neutrophil count in the blood is often encountered in the first few days of treatment in many serious infections and accompanies a favourable clinical response; this is usually followed by a gradual return of the count to normal levels, even while treatment is being continued. Such findings should suggest further observation, but not discontinuance of the drug, unless it no longer is indicated for treatment of the disease. On the other hand, in view of the importance of the problem and the paucity of thoroughly authenticated data, physicians should be encouraged to make complete blood studies before treatment with this or other potential bone-marrow depressants is initially undertaken, and again later, particularly before subsequent courses of treatment with such agents. Logistically, however, the probability of encountering abnormal findings that are significant and indicative of future serious trouble are extremely small, judging from the very low incidence of this serious complication. Initial counts, however, are significant in order to rule out antecedent blood dyscrasias.

Erythromycin and Carbomycin

The antimicrobial spectrum of these two antibiotics appears to be almost identical qualitatively, but against most of the susceptible strains of bacteria erythromycin appears to be appreciably more active than carbomycin. The antibacterial spectrum of both agents resembles closely that of penicillin, but they are said to be active also against rickettsias and against the psittacosis–lymphogranuloma–venereum group of organisms. Pharmacologically, erythromycin and carbomycin differ greatly. Oral administration of erythromycin, especially with alkali, yields rather high concentrations in blood and urine. Significant concentrations of carbomycin, however, are not readily demonstrable in the blood, except in patients with jaundice, and, although rather high concentrations are found in the bile, very little active carbomycin is recovered from the faeces and urine.

Erythromycin seems to be somewhat less effective than penicillin against most infections with Gram-positive organisms and much less effective against gonococcal infections. Its major usefulness has been in the treatment of staphylococcal infections, particularly those resistant to penicillin, aureomycin, and terramycin, and the results in such cases have, on the whole, been encouraging. Failures in patients with endocarditis have been associated with development of resistance in the staphylococci during the course of treatment. Similarly, the development of resistance seems to be the major cause of most of the failures of erythromycin treatment in cases of enterococcal and *Streptococcus viridans* endocarditis; only rarely have such cases responded favourably to treatment with this agent alone. In these cases, better results may possibly be obtained by the use of erythromycin in combination with penicillin, streptomycin, or bacitracin, which may increase the activity and delay or prevent the development of resistance in the infecting organism.

The results of the use of carbomycin in the treatment of infections with bacteria that are susceptible to it *in vitro* have, generally speaking, not been very favourable, and, on the whole, they have been quite inferior to those obtained with erythromycin in similar cases. Indeed, in the treatment of pneumococcal pneumonia the appearance of bacteriaemia and the development of purulent complications, including meningitis, during the course of treatment with maximum tolerated doses of carbomycin suggest that this antibiotic should be avoided at least in this disease. It has also proved disappointing in the treatment of staphylococcal infections. Of interest, however, are reports indicating that carbomycin may be effective in the treatment of amoebiasis and in cases of granuloma inguinale (Donovanosis).

Bacitracin, Polymyxin, and Neomycin

These three agents are grouped together because their inherent toxicity when they are used parenterally has greatly limited their use in systemic diseases. Each, however, has been successfully used by the intramuscular route in important and serious infections when others have failed.

Systemic bacitracin has proved particularly useful, alone or with penicillin or other antibiotics, in the treatment of a few cases of bacterial endocarditis and in other cases due to Gram-positive organisms resistant to other antibiotics. Occasional successes have also been reported in meningitis and brain abscess due to similar organisms; in these conditions it is said to be devoid of local irritation, thus permitting topical application, intrathecally, intraventricularly, and into brain abscesses. The local irritation from intramuscular injection, however, may be quite marked, but this is minimized by including procaine with the diluent and by limiting

individual injections to 25,000 units or less. The nephrotoxicity of bacitracin, which is inherently related to its activity, is generally transient; it has also been limited to some extent by improvements in manufacture, but chiefly by keeping the average daily dose in adults down to 100,000 units or less, maintaining the urine at a neutral or slightly alkaline *p*H, and avoiding systemic treatment or using it with great caution in patients who already have reduced renal function.

Polymyxin B, likewise, has found special uses, locally and systemically, in the treatment of infections with strains of *Pseudomonas* and other Gram-negative bacilli which are resistant to other forms of treatment. As with bacitracin, the nephrotoxicity has been either avoided or transient, or kept at a minimum by proper dosage, and in children the drug has not been much of a problem when properly used. The local irritation and slight fever from intramuscular injections has been found to be much lower in purified preparations of polymyxin B and more recently in preparations of polymyxin E. The paraesthesias, however, are still a particularly prominent feature of treatment in adults, but do not seem to be very important in infants and children.

Neomycin is probably the most toxic of these agents when used systemically, producing renal and auditory damage with sufficient frequency and severity to justify its use in this manner only under circumstances which warrant great risks. The toxicity is minor when the dose is kept at 1 g. a day and given for brief periods. When so used, it may be of value in some infections with organisms sensitive to this antibiotic, but considered to be resistant to other agents.

The major uses of bacitracin and also of polymyxin and neomycin, at present, seem to be their local application in the treatment of infected wounds and dermatological lesions. Their low irritating and sensitizing potential when used in this manner has made them especially suited for these purposes. Moreover, such usage is particularly appropriate because of the higher sensitizing potential of most of the antibiotics that are more commonly used for systemic therapy. The reports of such topical use, which have come primarily from dermatologists and surgeons, are generally favourable, but they are often difficult to evaluate. These antibiotics have been used separately and in various combinations, often all three of them together and sometimes with streptomycin. When so used they exert a powerful bacteriostatic and bactericidal effect on a wide range of bacterial species.

Each of these three antibiotics is also very poorly absorbed from the gastro-intestinal tract. Advantage is taken of this property for their use in reducing the bowel flora. Various combinations of bacitracin, polymyxin, neomycin, and streptomycin have proved as effective as any other agents previously used for this purpose. Neomycin in particular seems to be favoured at the moment by some authorities in this field because of its broad antibacterial range and its rapid action. It is less active than bacitracin against clostridia and other Gram-positive organisms, so that the two of them have been used successfully together. Bacitracin and polymyxin likewise cover a wide range of activity, which, however, does not include the *Proteus* organisms.

Special Uses

A few remarks about the use of antimicrobial agents in some selected situations may be appropriate, though it is appreciated that one can hardly do justice to those subjects in a presentation of this sort.

Urinary Tract Infections

First, in urinary tract infections, a critical survey of current reports suggests that there may be a declining efficacy of the available agents. This may be more apparent than real, and may be due in part to the fact that much more is expected of antimicrobial agents than is justified on the basis of their known activities. The cases in which there are partial or total failures keep returning, and temporary relief is followed by further relapses or reinfections, either with resistant strains or, more often, because the underlying and predisposing factors have not been or cannot be corrected. Eventually one is left with a group of patients who have residual infections which resist all available agents until some new one with a slightly different action appears. This may again give temporary relief. Infections with *Pseudomonas, Proteus,* and *Enterococcus,* and more recently an increase in *Aerobacter* infections, seem to be most frequently encountered in such resistant cases. A similar situation exists among patients with chronic bronchopulmonary suppurative lesions in which organisms not usually considered to be respiratory pathogens are now being found with increasing frequency as a result of the repeated elimination of the common respiratory pathogens by the use of increasing amounts and varieties of antimicrobial agents.

Bacterial Endocarditis

The problem of therapy in cases of bacterial endocarditis in which blood cultures are persistently negative has recently received special prominence because of the higher mortality in such cases as compared with that in patients with positive blood cultures. Needless to say, appreciation of the seriousness of this disease, of the need for prolonged and intensive treatment, and of the importance of a thorough knowledge of the aetiological agent is not only desirable but almost imperative for the proper conduct of such therapy. This is necessary not only for the choice of the agent but for the determination of dosage and duration of treatment; and it emphasizes the importance of making every effort to identify the aetiological agent before treatment is begun.

In patients in whom bacterial endocarditis is at all suspected, it is particularly important, therefore, that the usual tendency to give penicillin or other antimicrobial agents be avoided until proper blood cultures have been taken. Such treatment may not only reduce the chances of subsequently obtaining positive blood cultures but may even render it impossible to do so. Moreover, there is evidence that such treatment, which is usually inadequate to produce a cure, may appreciably increase the difficulty in subsequently obtaining a cure even when positive blood cultures are obtained and large doses of properly selected agents are then given. However, after proper cultures have been made and while awaiting the results, it may be desirable or even imperative to begin treatment. In such cases the preferred antimicrobial treatment would seem to consist of large doses of penicillin given in the aqueous form by intermittent intramuscular injection and supplemented by moderate doses of streptomycin. The dose of penicillin can be increased steadily after several days if the response still seems inadequate, and probenecid may also be added. If evidence of infection continues, and no bacterial agent has been forthcoming to provide the basis for a rational change, treatment becomes essentially a matter of trial and error, and the present tendency to use multiple agents often prevails.

Clinical and bacteriological cures in a few cases of bacterial endocarditis of known and varied aetiology have been reported during treatment with chloramphenicol, terramycin, or aureomycin, particularly the latter, but these agents are not the antibiotics of choice in such infections. In the majority of reports of their use in such cases, marked inhibition of the infection, with clinical improvement and negative cultures, occurred—sometimes for prolonged periods during treatment—only to be followed by relapses of symptoms and bacteriaemia after these drugs were discontinued. In most of these cases the subsequent administration of the same antibiotic in combination with others, or the use of other combinations, particularly massive doses of penicillin plus streptomycin, has resulted in cures. One possible cause of failures of treatment with aureomycin and terramycin has been the difficulty of sustaining treatment with the desired doses for long periods. From current clinical indications this may be more feasible with tetracycline, and better results may be forthcoming in some cases if, indeed, this was an important factor in the earlier failures. Development of resistance in originally sensitive organisms during

the course of treatment has only rarely been found responsible for failures of therapy with these antibiotics, in contrast to the findings in cases treated with erythromycin.

Meningococcal Infections

Meningococcal infections appear destined to increase in prevalence during the coming years. There is no evidence to indicate that the sulphonamide drugs, particularly sulphadiazine, have as yet been displaced as the most effective agents in the treatment of infection with this organism. The occurrence of sulphonamide-resistant strains, if they have been encountered, must be extremely rare. However, the general tendency of physicians to inject procaine penicillin, or some other repository form of penicillin, into all patients with fever may result in an increase in the number of failures in the treatment of this disease. Moreover, although the use of huge intramuscular doses of soluble preparations of penicillin may be effective in the treatment of meningococcal meningitis, such a regimen hardly seems warranted and can hardly be recommended as the treatment of choice if the sulphonamides are equally or more effective.

Hormone Therapy

In connexion with the problem of meningococcal infections, any increase in their prevalence is inevitably associated with an increase in the occurrence of cases of the so-called Waterhouse–Friderichsen syndrome. Since the adrenal hormones have been generally accepted as an integral part of the treatment of this condition, it seems appropriate to raise the question of the use of adrenal hormones in infection. This subject was reviewed by Thomas,[1] and more recently by Kass and Finland.[2] Among certain groups of clinicians interested in this subject there are apparently widely divergent views which, because of the paucity of adequately controlled data, are quite difficult to reconcile. There are those who feel that such hormones should be given to all patients with severe infections in order to hasten the symptomatic recovery while awaiting the more lasting and curative effects of antibiotics. Others, aware of the increase in severity of infections which may result, and which may reduce the effectiveness of antimicrobial therapy, have felt that the risk is unwarranted, unnecessary, and only rarely justified, and that the few unfavourable results may more than balance any temporary and apparent advantages. The middle course is taken by those who, recognizing the dangers, have limited the use of the hormone treatment to the first day or two while antibiotics are being given, in the hope of obtaining the maximum benefits from the hormones while incurring a minimum of risks from their use.

There is general agreement that in experimental infections cortisone and A.C.T.H. enhance infections of almost all types. It is also clear that this enhancement of infection or decrease in resistance to infection is quite non-specific with respect to the microbial aetiology of the disease and is even independent of multiplication of the organisms themselves, since it can be demonstrated in the increase in necrotic action of bacterial toxins alone. There is also abundant evidence that many types of human infections are aggravated by treatment with A.C.T.H. and cortisone, and that such treatment also gives rise to spontaneous infections with organisms that are normally saprophytic, or renders clinically active other infections which may be latent. This enhancement of infection, however, is associated with certain non-specific alterations in the clinical manifestations of infection which include a drop in temperature and increase in the general appearance of well-being which are known to be the direct results of hormone therapy and which occur in spite of advancing infections. These non-specific effects make it difficult and sometimes impossible to evaluate the course of the infection or to recognize the occurrence of new and complicating infections.

Proper evaluation of the hazards involved in the hormone therapy of infections is still not possible, and awaits carefully controlled clinical and bacteriological studies on a large number of cases. The difficulties of evaluating results of such usage are increased by the fact that full advantage is usually taken of the beneficial effects of antibiotics during the administration of the hormones. Indeed, the realization of the prospect of enhancing an infection generally leads to the use of multiple antibiotics, and in large doses, along with the hormones.

With respect to the specific problems presented by the Waterhouse–Friderichsen syndrome it is well to point out that in spite of the readiness of most clinicians to admit the need for adrenal hormones in this condition there is little or no acceptable proof that an adrenal insufficiency is a major or an important factor in this disease. Certainly it has never been clearly demonstrated that there is any residual adrenal insufficiency in patients who recover from this disease with or without hormones. There is also little evidence that there is any specific difference in adrenal activity in this disease as compared with that in other severe infections or toxaemias in which there is definite evidence of *increased* adrenocortical activity. With respect to the hypotensive or shock-like phase of this syndrome, the question may properly be raised whether this may not be better managed by the use of agents specifically directed against the hypotension, while awaiting the specific curative effects of the antibacterial agents.

Prophylaxis

There is little doubt that, in the U.S.A. at least, the total volume of antimicrobial agents used in prophylaxis or for minor and irrelevant indications exceeds by manyfold the total amount used in the treatment of infections for which they are specifically indicated. In the recent report on the use of one agent at a large community and teaching hospital it was revealed that 65% of the patients received that agent solely for prophylaxis, and many of the same patients had been given other antibiotics at the same time. It is obviously impossible to evaluate such usage. A few words concerning some of the more specifically directed prophylactic uses of antimicrobial agents may be in order.

In evaluating prophylaxis it is desirable to know, first, the objective and how that can best be measured; second, the best method of accomplishing that objective; and, third, the price that must be paid, not particularly in dollars and cents, but in terms of serious side-effects. As to the objectives, one may differentiate several types of uses.

(1) Mass prophylaxis of short duration and for a specific purpose, as in the use of sulphadiazine in the elimination of meningococcal infections and carriers.

(2) Mass prophylaxis on a continuous basis, as in the attempt to minimize acute respiratory infections through the administration of sulphadiazine.

(3) Individual prophylaxis on a continuous basis, as in the use of sulphonamides or penicillin in the prevention of recurrences of rheumatic fever indirectly through the prevention of haemolytic streptococcal infections.

(4) Individual but brief prophylaxis against specific infections, as in the use of oral penicillin following venereal exposures or perhaps in the prevention of ophthalmia neonatorum.

(5) Individual prophylaxis, given in a more prolonged or intensive course, in the hope of preventing various infections, as in the use of antimicrobial agents: (*a*) in the preparation for bowel resections or immediately after such resections; (*b*) in women during or after long and complicated delivery; (*c*) after catheterization or instrumentation of the urinary tract, or after operations in this region; (*d*) in relation to tooth extraction or dental manipulations in patients with valvular or congenital cardiac defects in the hope of preventing subacute bacterial endocarditis; and (*e*) during the early phases of management of burns and other potentially infected surface wounds.

The use of antibiotics in the treatment of common colds and acute simple undifferentiated respiratory diseases or in non-streptococcal pharyngitis may perhaps also be included in the latter category because this amounts essentially to the prophylaxis of complicating bacterial infections. On the other hand, early treatment of streptococcal infections

[1] *Ann. Rev. Med.*, 1952.
[2] *Ann. Rev. Microbiol.*, 1953.

as a means of preventing attacks of rheumatic fever or glomerulonephritis may be considered in a different category, since one is here dealing with an already established infection for which one is administering specific treatment.

The different types of prophylactic uses do not lend themselves equally to proper evaluation. From available data, however, one may easily conclude that the two most successful of these uses have been the mass prophylaxis of meningococcal infections by the administration of a short course of sulphadiazine and the individual prophylaxis of gonococcal infections by the use of single oral doses of penicillin immediately following exposure. The success of these procedures is based on the fact that in these situations one is dealing with specific bacteria against which the prophylactic agents have proved efficacy to a marked degree under the particular conditions in which they are used. Moreover, under these conditions the untoward effects are minimal.

The success of individual prophylaxis of streptococcal infections and recrudescences of rheumatic fever by continuous administration of sulphonamides or penicillin is more difficult to measure, but seems fairly well established. Although this involves a greater risk of untoward effects, that seems warranted in view of the nature of the disease one aims to prevent. In this connexion it may be pointed out that the choice of the optimum agent has not been clearly defined. It may therefore be worth considering that, although penicillin may be slightly more effective for the purpose, it may still be preferable to use another agent, like a sulphonamide, which is adequate for the purpose. Should an infection then occur it is less likely to be resistant to penicillin, which would then be available, and more likely to be effective in the treatment of that infection.

Mass prophylaxis on a continuous basis has been only partially successful, but for the purpose for which it was designed it has served as well as was possible at the time. Such continuous prophylaxis is inevitably accompanied by a much greater risk of untoward effects, some of which may be serious. The experiences with such usage in the U.S. Armed Forces during the second world war taught us the danger of the replacement of the prevalent flora by organisms resistant to the prophylactic agent being used. This phenomenon has more clearly been exemplified, on a different scale and under different circumstances, by the spread of penicillin-resistant staphylococci in hospitals where they are widely and continuously used.

In the experience with sulphadiazine prophylaxis during the second world war it was fortunate that the severe infections with sulphadiazine-resistant streptococci occurred just at a time when penicillin became available, so that the potentially serious consequence of the fact that sulphadiazine was no longer effective in these cases was mitigated by the use of penicillin. This emphasizes the importance of choosing for prophylaxis an agent which is effective, but which is different from the one that must be relied on for the treatment of severe infections that may arise during such prophylaxis.

Individual prophylaxis for specific purposes is of course the major excuse for the widespread use of antibiotics. It is also the most difficult to evaluate. No attempt will be made to do so, but a brief comment on one of the more accepted uses which is considered to be fully justified may be in order—namely, the use of penicillin during dental manipulations in patients with valvular or congenital heart disease for the prevention of bacterial endocarditis. Although the principle of this usage is generally accepted, there is considerable difference of opinion regarding the dosage to be used, whether it is necessary to give the antibiotic before the actual procedure, for how long before and for how long after that procedure. The controversies may stem from the fact that the objective is not entirely clear. For example, if the aim is to eliminate the potential blood-stream invaders from the dental foci it would require large doses given over a long period prior to the dental procedures; only a brief period of treatment would then be required after the actual operation, unless one were dealing with an infection which had not been entirely eradicated at the time, when resort must be had to more prolonged use of similar large doses. On the other hand, if the aim is merely to clear the blood stream of the organisms which invade just at the time of the dental procedure, a single relatively small dose given at or shortly before that time should suffice.

Obviously one cannot hope to prevent all blood-stream invasions from dental foci, since presumably such invasion takes place during inevitable daily procedures, such as the mastication of food and the brushing of teeth. If one should wish to prevent or to minimize the dangers of such invasions one might be tempted to use continuous therapy throughout the life of the individual. Of the extremes that have been advocated, the use of the single small dose reduces or prevents the immediate bacteriaemia and is obviously associated with the least risk of sensitization and other reactions, and also offers the smallest risk of replacing the oral or dental flora by the potential causative organisms of endocarditis, which may be resistant to penicillin, whereas the more prolonged treatment with the largest doses offers the greatest potential risks in these respects, although it may best serve the purpose of reducing or eliminating dental infections.

The final answer to this problem cannot be given, for there seems to be no acceptable evidence that any cases of bacterial endocarditis have actually been prevented by any type of prophylaxis. On the other hand, there are at least a few cases of bacterial endocarditis, fairly well authenticated, which have followed extractions under prophylaxis of various types. Of particular interest is the fact that in the patient who received the largest doses and for the longest period the endocarditis which followed was caused by the most resistant organism. Here is further support for the general idea that the prophylactic agent of choice for any given purpose should be different from the one on which it may be necessary later to place chief reliance for cure of infections that might occur. Put another way, a less active agent may suffice for prophylactic purposes but may not prove adequate for treatment, should that become necessary.

Omnibiotics

The physician in practice, and many of his patients as well, are constantly on the look-out for some simple substance or formula which can be applied with universal success. The busy practitioner is particularly desirous of having some major weapon on which he can always rely to be successful in all types of infections, and which would thus relieve him of the responsibility and trouble involved in the complicated or even simple diagnostic procedures. Whenever such a cure-all has been offered it has usually been grasped with enthusiasm and widely and indiscriminately applied. The disappointment which invariably has followed has always been proportional to the magnitude of the unwarranted promises and claims that had been held out. On the other hand, the discriminate choice of therapeutic agents only on the basis of proper indication and proved efficacy for the desired purpose, though perhaps more difficult to practise, may in the long run be less disappointing and more rewarding.

Summary and Conclusions

This has been an attempt to bring out in a critical manner some of the current problems in the use of the antibiotics at present available. Many of the opinions that have been expressed will undoubtedly meet with honest and justifiable disagreement, for they express only the deductions made by me on the basis of my own experience. There is one conclusion, however, with which few will dissent—namely, that there still remain many problems in the treatment and prevention of infectious diseases which have not been solved by the antibiotics at present available.

THE MORTALITY FROM CHILDHOOD TUBERCULOSIS IN SHEFFIELD

POSSIBLE CAUSES OF ITS DECLINE

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The purpose of this paper is to describe the recent decline in tuberculosis mortality in children in Sheffield, to consider some of the factors probably responsible for that decline, and to compare the results in Sheffield with those obtained in Great Britain and her other major cities.

Decline of Tuberculosis Mortality in Children

Sheffield

In 1924, 82 Sheffield children under 15 years of age died of tuberculosis. In the next ten years the number of annual deaths was more than halved, and in 1934 they fell to 29. At this point the improvement was halted, and between 1934 and 1947 no significant reduction occurred. The number of children who died of tuberculosis varied between 25 and 31 in the peace years, but rose higher in the war years and reached a peak of 39 in 1941.

After 1947 there was a dramatic fall in the tuberculosis mortality in children. In 1948 and 1949, 18 children died each year, in 1950 12, in 1951 6, and in 1952 only 2 (Table I). The death rate per 100,000 children under 15 years of age fell from 25 in 1947 to 1.8 in 1952, or 7% of the 1947 figure, representing a 14-fold reduction in five years.

TABLE I.—*Annual Number of Deaths from Tuberculosis in Children (0–14 years) in Sheffield, 1924–52*

Year	No. of Deaths	Year	No. of Deaths	Year	No. of Deaths
1924	82	1934	29	1944	37
1925	72	1935	28	1945	26
1926	80	1936	28	1946	25
1927	81	1937	31	1947	26
1928	71	1938	31		
1929	58	1939	35	1948	18
1930	53	1940	35	1949	18
1931	40	1941	39	1950	12
1932	44	1942	30	1951	6
1933	38	1943	38	1952	2

This sharp decline in tuberculosis mortality in children far exceeded both the decline of the overall tuberculosis mortality at all ages and the decline of mortality of children from other causes.

During the period 1934 to 1945 child deaths from tuberculosis amounted to between 7.2 and 10.4% of all deaths from tuberculosis at all ages, the proportion showing a tendency to rise during the war years. In 1947 8.8% of all the tuberculosis deaths in the city occurred in children, which was the same as the average in the three years preceding the war. After that time this proportion fell steadily, and in 1952 child deaths from tuberculosis amounted to only 1.6%. During the same period adult deaths from tuberculosis fell only to 46% of the 1947 figure (Table II).

The importance of tuberculosis as a cause of death in children was particularly evident in the age group 1 to 14 years. In 1944 deaths from tuberculosis in this group amounted to 21% of deaths from all causes, and in the first three post-war years the average annual figure was still 16.8%. In these years tuberculosis was second only to accidents as a cause of death. After 1947 child deaths from all causes between 1 and 14 years of age fell to one-half, but, whereas the number of deaths from all causes other than tuberculosis fell to three-fifths, deaths from tuberculosis fell to one-tenth and accounted for only 3.5% of all deaths (Table III).

TABLE II.—*Annual Deaths from Tuberculosis at All Ages and in Children Under 15 Years of Age. Child Deaths as a Percentage of Deaths from Tuberculosis at All Ages. England and Wales and Sheffield*

Year	England and Wales			Sheffield		
	All Ages	Children 0–14	Child Deaths (%)	All Ages	Children 0–14	Child Deaths (%)
1934–6* ..	28,693	2,904	10·4	385	28	7·2
1937–9* ..	26,297	2,311	8·5	361	32	8·8
1940–2* ..	27,096	2,527	9·0	371	35	9·4
1943–5* ..	24,245	2,198	9·0	325	34	10·4
1946 ..	23,388	1,914	8·2	301	25	8·3
1947 ..	23,075	1,955	8·4	294	26	8·8
1948 ..	21,665	1,562	7·2	255	18	7·0
1949 ..	19,721	1,148	5·8	264	18	6·8
1950 ..	15,969	909	5·7	189	12	6·4
1951 ..	13,806	831	6·0	181	6	3·4
1952 ..	10,567	—	—	127	2	1·6

* Triennial figures are yearly averages.

TABLE III.—*Annual Number of Deaths (1–14 Years) from Tuberculosis and All Causes. England and Wales and Sheffield* 1944–52

Year	Deaths from Tb		Deaths from All Other Causes		Total Deaths		Tb Deaths as % of All Deaths	
	E.&W.	S.	E.&W.	S.	E.&W.	S.	E.&W.	S.
1944 ..	1,803	32	11,672	120	13,475	152	13·3	21·0
1945–7*	1,716	22	9,084	109	10,800	131	15·9	16·8
1948 ..	1,316	17	7,537	100	8,853	117	14·9	14·5
1949 ..	985	17	7,287	97	8,272	114	11·9	14·9
1950 ..	785	10	6,203	62	6,988	72	11·2	13·9
1951 ..	732	6	6,500	62	7,232	68	10·1	8·8
1952 ..	—	2	—	54	—	56	—	3·5

* Yearly average.

Great Britain

Similar trends in mortality could be observed in England and Wales and in Scotland during most of the period under review. In England and Wales the general tendency of improvement slowed down several years before the war, and between 1935 and 1947 tuberculosis was still responsible for from 2,000 to 3,000 deaths each year, the death rate per 100,000 children being 28.5 in 1935 and 21.4 in 1947. After 1948 the rate of fall became substantially accelerated, and in 1951 831 children died of tuberculosis, the death rate being 8.5 per 100,000 (Table II). The tuberculosis death rate of Sheffield children was consistently higher than that of England and Wales up to and including 1950, but in 1951 the Sheffield rate fell to three-fifths of the national rate, although Sheffield's adult tuberculosis mortality rate was still 12% above the national average. The official tuberculosis mortality figures of children in England and Wales for 1952 have not yet been published. Available unofficial information suggests, however, that in 1952 Sheffield's rate will be about one-third of the national rate.

In Scotland the situation has generally been much less favourable, and in 1947 the tuberculosis death rate in children was 46 per 100,000, compared with 21 in England and Wales and 25 in Sheffield. Since then the position has greatly improved and the mortality rate fell to 16 in 1951 (England and Wales = 8.5), and to 10 in 1952 (Table V). This last figure, however, is still more than five times as high as that of Sheffield. In spite of Scotland's much higher mortality rate in 1947, the rate of fall up to 1952 was three times slower than that of Sheffield.

Compared with London and the other major English cities with a total population of over 500,000 and a child population of over 100,000, Sheffield occupied a middle position until 1950. In 1951 Sheffield's tuberculosis mortality rate for children fell below the others, and in 1952 it was between one-fifth and two-fifths that of the other cities. Sheffield's rate was two-fifths that of the combined rate of the six next largest cities with a total population of 280,000 to 500,000 and a child population of 60,000 to 100,000, and was below that of any one of them (Table IV). Among these latter six the rates of Nottingham, Bristol, and Leicester were particularly favourable. In each of these major cities and in the two major cities of Scotland the mortality rate was reduced from three to five times between 1947 and 1952. In Sheffield the reduction was fourteenfold. In spite of great improvements, Glasgow's 1951 mortality rate of 20 per 100,000 was still eleven times higher than that of Sheffield (Table V). When the 1951 and 1952 death rates are combined the differences between Sheffield and most other major cities in Great Britain are statistically significant (Table VI).

TABLE IV.—*Annual Mortality Rate from Tuberculosis of Children aged 0–14 Years per 100,000 Living Children in England and Wales and in Their Major Cities*

Year	England and Wales	London (A.C.)	Birmingham	Liverpool	Manchester	Sheffield	Leeds	The Next 6 Cities*
1945	25	20	24	37	36	26	26	29
1946	22	25	20	30	27	24	18	23
1947	21	20	27	32	25	25	21	22
1948	17	15	23	30	21	17	15	20
1949	12	9	14	21	12	17	13	16
1950	9·4	6·0	8·7	20·0	10·1	10·5	8·2	11·7
1951	8·5	6·6	12·1	15·8	10·7	5·3	10·9	8·5
1952†		4·8	5·3	8·5	8·0	1·8	4·6	4·9

* Bristol, Nottingham, Kingston-upon-Hull, Bradford, Newcastle-upon-Tyne, Leicester.
† Provisional figures.

TABLE V.—*Annual Mortality Rate from Tuberculosis of Children Aged 0–14 Years per 100,000 Living Children in Scotland, Glasgow, and Edinburgh*

Year	Scotland	Glasgow	Edinburgh
1945	45	77	40
1946	46	75	38
1947	46	78	36
1948	32	56	36
1949	23	44	11
1950	18	38	11
1951	16	30·6	10
1952*	10	20·5	7·8

* Provisional

TABLE VI.—*Statistical Probability that the Differences Between Sheffield and other Cities are Due to Chance, Expressed in Percentages*

City	Child Population† (in Thousand)	Number of Child Deaths from Tuberculosis in 1951 and 1952	Probability %
London	660	74	17·2
Birmingham	260	46	0·4
Liverpool	210	50	0·1
Manchester ..	160	30	0·7
Sheffield	110	8	—
Leeds	110	17	7·2
Next 6 English cities combined* ..	450	58	6·8
Glasgow	260	136	<0·1
Edinburgh	100	18	3·0

* Bristol, Nottingham, Kingston-upon-Hull, Bradford, Newcastle-upon-Tyne, Leicester.
† 1951 Census figures.

Causes of Decline of Tuberculosis Mortality in Sheffield

It is now necessary to consider the various factors which might have been responsible for such a great decline in the tuberculosis mortality in children in the last five years in Sheffield. Among the possible factors were a change in the natural course of the disease, which may have taken on a more benign form; the effect of favourable trends in the environment; the effect of more efficient treatment; and, finally, the effect of active measures to eradicate the disease. Unknown factors may also have played a part.

Changes in the natural history of the disease in a short space of five years could only be minimal, and this factor need not be considered further.

Socio-economic Factors

It is difficult to estimate the influence of the changes in the living standards of the population. There is no evidence, however, that in the last five years the standard of living has risen to any great extent. The diet of the community was remarkably constant, the level of employment was uniformly high, but the housing conditions were bad and showed only slight improvement. There was a great deal of overcrowding, and many families lived in condemned houses or in houses which would have been condemned long ago had it not been for the housing shortage. The medical officer of health has made great efforts in the last 28 years to provide adequate housing for families with a sputum-positive member. Unfortunately, owing to the great shortage of houses, he was able to secure the rehousing of only those families in which there were small children and in which there was overcrowding in the statutory sense. The standards of epidemiological need had to be set very strictly, and, even so, the rehousing of those most in need could often not be secured until after the children became infected. In the last seven years an annual average of 68 tuberculous families have been rehoused. This rate has slowed down in recent years, and the figure fell to 28 in 1952. This rehousing policy may well contribute to the maintenance of a moderately low basic level of tuberculosis mortality, but there is no evidence that the recent rapid drop was due to this factor. Further evidence that improvements in the social conditions were probably not of major importance in recent years is presented below.

Effect of Specific Treatment of Tuberculous Children

The third possible factor in the reduction of mortality is the more efficient treatment of tuberculous children and adults since the introduction of streptomycin and other new drugs and methods of treatment. Treatment of infected children may directly save lives, while the treatment of infectious adults may prevent tuberculous infection in children.

Of these last two factors the effect of treatment of the fatal forms of tuberculosis in children is much more obvious, and it is relatively easy to assess its role quantitatively. The beginning of the recent fall in mortality coincided with the advent of streptomycin at the end of 1947. In the five years from 1948 to 1952, of 45 Sheffield children treated in the Sheffield Children's Hospital for tuberculous meningitis or miliary tuberculosis 32 recovered; of over 20 other Sheffield children treated elsewhere for these condi-

TABLE VII.—*Number of Children (0–14 Years) who Died of Tuberculosis and Who Were Successfully Treated for Fatal Forms of Tuberculosis. Sheffield, 1945–52*

Year	No. Died	No. Successfully Treated	Total
1934	29	—	29
1945	26	—	26
1946	25	S.M. —	25
1947	26	2	28
1948	18	5	23
1949	18	B.C.G. 7	25
1950	12	2	14
1951	6	10	16
1952	2	8	10

tions during the same period unfortunately only two survived. If one adds to the deaths from tuberculosis in each year the number of children who contracted tuberculous meningitis or miliary tuberculosis but survived, one obtains a close estimate of the minimum mortality which would have resulted without the use of streptomycin and the newer drugs (Table VII). It is apparent that the number of deaths in 1945 to 1949 and in the last six years before the war would have been strikingly similar. The fall in deaths in 1948 and 1949 was therefore apparently largely due to the streptomycin treatment of children suffering from meningitis and miliary tuberculosis. The figures from 1950 onwards suggest, however, additional factors of equal or greater importance.

Effect of Specific Treatment of Adults

One of these possible factors is the earlier diagnosis and the more effective treatment of tuberculous adults with streptomycin and other methods. It is difficult to assess quantitatively the exact role of this factor. Streptomycin undoubtedly reduced the mortality of adults and rendered more infectious cases sputum-negative more quickly, but it saved the lives of many advanced cases who live in a chronically sputum-positive state, possibly with resistant organisms and infecting others. The introduction of mass miniature radiography helped to detect active cases of tuberculosis at a relatively early stage of the disease. The fall in the tuberculosis mortality rate in adults in Sheffield to 46% of the 1947 figure already mentioned was, however, much less than that obtained in children (see Chart). It is of

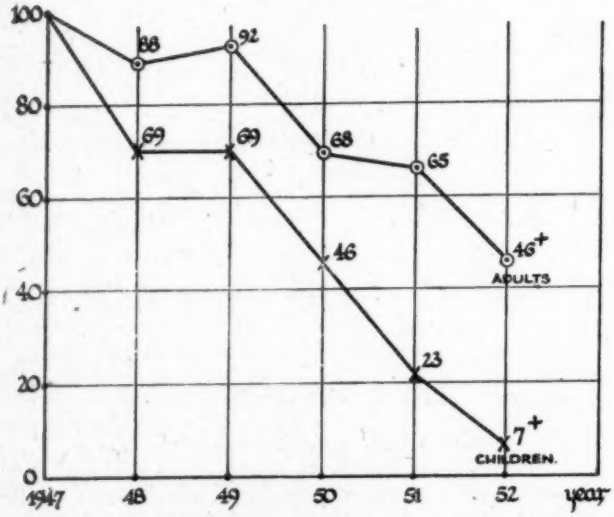

Chart showing the reduction of tuberculosis deaths in adults (15 years+) and children (0–14 years) in Sheffield, 1947–52. Comparative mortality indices, 1947=100. *Provisional figures.

interest that the rate of reduction in adult mortality was strikingly similar in the six largest cities of England and Wales, including Sheffield, and in the two largest cities in Scotland. The rate of reduction of deaths in children exceeded that of adults everywhere. Whereas, however, the ratio of reduction in favour of children in the other major cities was two to one or less, in Sheffield it was 6.5 to one (Table VIII).

TABLE VIII.—*Comparative Mortality Indices for Tuberculosis in Children and Adults for* 1952. 1947=100

City	Adults	Children	Ratio A/C
London	46	24	1·9
Birmingham ..	43	20	2·1
Liverpool ..	52	27	1·9
Manchester ..	49	32	1·5
Sheffield	46	7	6·5
Leeds	35	22	1·6
Glasgow	49	25	2·0
Edinburgh ..	41	21	2·0

It seems, therefore, that so far the more efficient treatment of adults has played only a minor part in the reduction of child mortality in Sheffield. There is no doubt, however, that the ultimate eradication of tuberculosis in children will depend chiefly on the early diagnosis, quick segregation, and effective treatment of tuberculosis in adults, just as the prevention of tuberculosis in children will contribute to the disappearance of tuberculosis in adults.

Preventive Measures

Finally, we must consider the effect of preventive measures. Milk-borne infection played very little part in the tuberculosis mortality of Sheffield children after the war. Practically all milk consumed within the city was pasteurized, and over 95% of the cases of tuberculous meningitis treated in the Children's Hospital between 1947 and 1952 were due to the human type of organism.

Up till 1949, however, very few facilities were available for segregation of children living in tuberculous households. In the course of an investigation of the contact history of 150 cases of tuberculous meningitis and miliary tuberculosis (Lorber, 1950) it was suggested that a great deal more could be done to prevent tuberculosis in children and to diagnose tuberculosis earlier in those who had already contracted the disease. Early diagnosis of meningitis and of miliary tuberculosis promised a considerable saving of lives, especially in children under 3 years of age. Over a third of our cases of tuberculous meningitis belonged to this group, and diagnosis was more often delayed in babies than in older children.

Work of a Contact Clinic for Babies and Small Children

In 1949 we therefore approached Dr. Turner, the chest physician of Sheffield, and asked for co-operation in opening a contact clinic for the younger age groups, in which the mortality was highest. This was agreed to, and it was accordingly arranged that all children aged 2 years or under who were in contact with notified cases of tuberculosis should attend a contact clinic at the Children's Hospital. In 1952 this age limit was extended to include those between 2 and 3 years old at the time of their first examination. Most of the older children remained the chest physician's responsibility, but we cared for many who were referred directly to us. The chest physician sent us periodically a list of children, giving brief details of the nature of contact, and it was our responsibility to call upon, examine, and look after these children. The chest physician also allowed us access to the records of the chest clinic, to ensure fuller co-operation in the service. Dr. Llywelyn Roberts, the medical officer of health for Sheffield, has given us great support by kindly allowing us to use the services of the city health visitors.

The organization of the clinic was as follows. The parents were sent a preliminary letter asking them to bring their child for examination at the Children's Hospital and giving the reason for this. They were also informed that a health visitor would call on them four days before their hospital appointment to explain the position in more detail and to apply a skin test. These arrangements were set in motion immediately we received a notification, so that all children were offered an appointment within a week. The health visitor then applied the tuberculin-jelly test and gave appropriate instructions. She also visited, as often as necessary, all those who failed to keep their appointments. From 1952 onwards a research assistant called at the houses of persistent absentees so that no child should miss a medical examination and so that continuity of supervision should be ensured. The family doctor was fully informed of the circumstances of the child's attendance and of our findings. We discussed with him our plans for the child's management, and told him about subsequent developments. In the case of tuberculous children, he was reminded of the possible serious significance of relatively trivial symptoms, which might mean the beginning of meningitis. The first

clinic was held in July, 1949, and up to the end of 1952 some 550 young children had attended at least once.

In the case of tuberculin-negative infants (the largest group) importance was attached to the instruction of parents in the methods of preventing infection when contact was inevitable. Immediate separation from contact, however, could usually be arranged. The index case was often already in a sanatorium or was just about to be admitted. In other cases permanent separation was possible without breaking up the family. In yet others, temporary separation could be arranged with their own relations. If this was not possible the infants were admitted to a small private nursery at the cost of the public health authority.

When B.C.G. became available vaccinations were started on the first possible day—October 6, 1949. By the end of 1952 we had vaccinated over 300 tuberculin-negative infants, including those born at the Jessop Hospital for Women who were in potential future contact with known cases of tuberculosis. Babies born of tuberculous mothers at the hospitals of the regional board were vaccinated by the chest physician, as were most of the older children. Up to the end of 1952 1,164 Sheffield children had been vaccinated—a relatively small number, representing 1% of Sheffield's child population of 110,000.

Separation from contact from active cases of tuberculosis was insisted upon for at least six weeks before vaccination, and again until tuberculin conversion had taken place. Separation is important if B.C.G. vaccination is not to fall into disrepute. One Sheffield boy who was vaccinated elsewhere without separation from contact developed tuberculosis of a hip-joint and pulmonary tuberculosis.

Babies and small children to the number of 104, or less than one-fifth of the total who attended, were already tuberculin-positive at their first visit or were converted spontaneously before protective measures could be taken. The management of these children was strictly conservative. Once they were infected it was not thought necessary to separate them from contact. They were cared for throughout as out-patients, unless illness or social reasons necessitated temporary admission to hospital. Everything possible was done to ensure the children's adequate nutrition, vitamin intake, and home care, and we provided financial help, bedding, and other services. When it was felt to be safe, usually after one year of observation, the children were sent away for long holidays by the seaside or in the country. Streptomycin was not used, except in those who developed tuberculous meningitis or miliary tuberculosis, and the results appear to justify this policy. In spite of the very young age at which these babies contracted tuberculosis, only a single child died of tuberculosis* in four years, and his death should have been prevented. This tuberculous infant had a short episode of irritability with vomiting. He was admitted, and his cerebrospinal fluid showed minimal deviation from normal, consistent with "serous tuberculous meningitis." He made a rapid spontaneous symptomatic recovery and the C.S.F. returned to normal in a few days. He remained well for four months, but then headache and vomiting recurred. His own doctor advised against taking him to hospital, "to save the child an unnecessary lumbar puncture." Several days later he developed an uncontrollable status epilepticus and died shortly after arrival in hospital, death being due to advanced tuberculous meningitis.

Effect of Earlier Diagnosis of Tuberculous Meningitis

Six other babies with primary tuberculosis who attended the clinic developed tuberculous meningitis while under observation. All were diagnosed within 24 hours of their first symptoms and all made a good recovery with streptomycin treatment. Another child developed miliary tuberculosis and is making satisfactory progress.

During the three years from 1949 to 1951 we treated 78 children suffering from tuberculous meningitis in the department of child health. Of our patients 60 came from outside Sheffield, and of these 25, or about two-fifths, survived, while of the 18 Sheffield children 14, or three-quarters, recovered, with a minimum period of observation of 23 months from the beginning of treatment. The better results in Sheffield children may be attributed to the earlier diagnosis of tuberculous meningitis, which we think was helped by the contact clinic and the intimate knowledge gained of the tuberculous babies of the city.

*Another child died of bulbar poliomyelitis. This diagnosis was confirmed at necropsy.

Discussion

Even if streptomycin had not been available for the treatment of tuberculous meningitis and miliary tuberculosis and all 10 Sheffield children who in 1952 developed these conditions had died, the death rate would have been only 9 per 100,000, compared with a rate of 25 per 100,000 in 1947. This hypothetical death rate is almost the same as was the actual death rate in two large neighbouring cities and in the whole of Scotland in 1952 and in England and Wales in 1951. These figures indicate the progress of the preventive aspects of the work in the last few years. Between 1947 and 1950 the rate of reduction of child mortality from tuberculosis was very similar in England and Wales, in Scotland, and in the eight major cities, including Sheffield. Since then the rate of reduction has slowed down, except in Sheffield, when it was accelerated (Table IX). In Scotland, London, Birmingham, Manchester, Leeds, Glasgow, and Edinburgh the mortality rate in 1952 was over one-half of the 1950 figure; in Liverpool it was two-fifths, and in Sheffield only one-sixth.

TABLE IX.—*Comparative Mortality Indices for Tuberculosis in Children for* 1950 *and* 1952. 1947=100

	1950	1952
England and Wales	45	—
Scotland	39	22
London	30	24
Birmingham	35	20
Liverpool	64	27
Manchester	41	32
Sheffield	46	7
Leeds	41	22
Glasgow	45	25
Edinburgh	29	21

Unfortunately, because of the vagaries of notifications, it is impossible to obtain accurate and comparable figures of tuberculosis morbidity in children. In Sheffield there has been a growing tendency to discover and notify an increasing proportion of the tuberculous children. In the five years from 1947 to 1951 inclusive an average of 240 children were notified (range 226 to 253), but in 1952 this number fell by one-third to 163, providing some further evidence of the success of the preventive measures, and also indicating that there is much room for further improvement.

It is not possible to state just how much each measure contributed to the fall in tuberculosis mortality in Sheffield children. It appears probable that B.C.G. vaccination of susceptible contacts was a factor, because not one of them has developed clinically or radiologically detectable tuberculosis so far, and none have died, although they were all allowed to resume contact after successful conversion. It is of interest that such a relatively small number of vaccinations, involving only 1% of the child population in 3½ years, could be effective, because it appears that most of those in need were actually vaccinated. These findings suggest that by the earliest possible examination of susceptible child contacts, their quick segregation, and their subsequent vaccination, further reduction of morbidity and mortality can be anticipated, and that mass B.C.G. vaccination of small children may not be necessary under the conditions at present prevailing in this country.

It would be unwise to attach too much importance to the specially low figures obtained in 1952, unless they are regularly repeated, or even improved upon, in subsequent

years. Nevertheless, the trend of mortality has been so consistently downward in the last five years that, subject to increasing vigilance, one may reasonably hope for further progress in this sphere. In the first half of 1953 only one Sheffield child died of tuberculosis. A careful examination of the local situation leads one to conclude that complete eradication of tuberculosis mortality in children is possible in the near future, and that any deterioration could only be the direct result of relaxation of our efforts.

There is yet much to be done in the field of tuberculosis prevention. In our experience the first and basic necessity is the acquisition of a sense of urgency by all those who deal with any aspect of tuberculosis. This is a difficult task when confronted with a disease which is always with us and the progress of which is usually measured in months and not days. A few weeks' delay in contact examination and in arranging for the segregation of infectious cases may greatly diminish the efficiency of the preventive services and of a B.C.G. vaccination programme, because the contacts of the most infectious cases will already have contracted tuberculosis before adequate steps can be taken to protect them. Complacency is our greatest enemy.

Meanwhile, with reasonably early diagnosis of tuberculous meningitis and of miliary tuberculosis, and with adequate treatment, most patients should now be saved. Of 20 patients suffering from tuberculous meningitis who were admitted from a wide area to the department of child health during 1951 and who were conscious on admission, 18 survived, with a minimum period of observation of 21 months. Out of 14 cases of uncomplicated miliary tuberculosis in children under our care after 1947 none has died. These cases must be treated as medical emergencies in a fully equipped centre. Had this been done in the case of the two deaths in 1952 these deaths might not have occurred.

It is not the purpose of this paper to discuss in detail the principles of the prevention of tuberculosis. These are well known, and much lip service is paid to them. Nevertheless everyday experience shows serious gaps in the application of these principles. Lack of hospital beds and shortage of nurses for the care of tuberculous adults are only part of the trouble, which requires urgent remedies on a national level. Case-finding methods could be further intensified. In this respect it is regrettable that a positive tuberculin reaction in a small child is not admissible for notification if this is the only evidence of his disease. This regulation deprives the chest physician of an excellent case-finding method. Contact examinations should be extended beyond the immediate household.

Education of the general public and of tuberculous patients is still far from adequate, and there is much complacency regarding the supposed lack of infectivity of sputum-negative cases. It is only in the application of the fundamental principles of tuberculosis control that the eventual eradication of this disease will be possible. Meanwhile, the judicious use of B.C.G. for susceptible contacts and the skilful treatment of tuberculous children should lead to the elimination of deaths from tuberculosis in children. Our experience suggests that this may be best achieved by the intimate co-operation of the paediatric services with the chest clinic and the public health authorities.

Sources of Information.—The data on which this paper is based were obtained from the Annual Reports of the Registrar-General of England and Wales and from the Registrar-General's personal communications for 1951 and 1952; from information obtained from the Chief Medical Officer of Health for Scotland and from the medical officers of health of those cities for which statistics are here provided; and from the records of the Chest Clinic, Sheffield. Death rates for 1951 were calculated on the basis of the provisional estimates of population in the 1951 Census and for other years on intercensal estimates. As the previous census was held 20 years ago, and as the war caused great dislocation of the population, these estimates are subject to error, but not sufficient to affect appreciably the calculated mortality rates. Any degree of error so introduced would apply to all areas in the same way. For the reason of this possible error, however, the absolute number of deaths was used for the various calculations wherever possible.

Summary

The tuberculosis mortality figures of Sheffield children for the last 30 years are presented. The number of annual deaths did not fall between 1934 and 1947, but after that the death rate dropped 14-fold in five years—from 25 in 1947 to 1.8 per 100,000 in 1952. In 1952 only two Sheffield children died of tuberculosis. This decline of tuberculosis mortality in children far exceeded that in adults and also the decline of mortality in children from all other causes.

In Great Britain as a whole, as well as in all her other major cities, the fall was considerable during the same period, but was less than fivefold everywhere except in Sheffield. The tuberculosis mortality rates for 1951 and 1952 in Sheffield were better than in any other major city in the country.

The possible causes for the recent rapid improvement in Sheffield are discussed and analysed. It is shown that the successful treatment of otherwise fatal forms of tuberculosis in children since streptomycin became available was responsible for this improvement up to and including 1949. Since 1950, preventive measures—namely, intensified contact examinations, segregation, and B.C.G. vaccination of children in tuberculous families and households—may have been as important as streptomycin treatment in the progressive reduction in mortality. In this connexion the work of a tuberculosis contact clinic for small children has been outlined.

Further reduction of tuberculosis morbidity, and the eradication of tuberculosis mortality, are believed to be possible with increasing effort and vigilance. The fundamental methods of tuberculosis control, assisted by B.C.G. vaccination and the effective chemotherapy of the otherwise fatal forms of tuberculosis in children, should quickly lead to the elimination of deaths from this cause in children.

I acknowledge with much pleasure my indebtedness to Dr. H. Midgley Turner, consultant chest physician of Sheffield, for his constant help with the work of the Contact Clinic and for the access to the records of the Chest Clinic; to Dr. Llywelyn Roberts, medical officer of health for Sheffield, for his support of the clinic by allowing his health visitors to assist in the work, for his suggestions, encouragement, and for help in obtaining much information for this paper and for his criticism; to Miss Littlewood and the late Miss Liddle, superintendent health visitors, and their staff for co-operation in contact tracing; to Miss Crowley, the lady almoner of the Children's Hospital, Sheffield, for her interest and assistance in the social aspects of the work of the Contact Clinic; and to Dr. Elizabeth Sutherland, who assisted in the contact examinations in the second half of 1952.

I would like to thank Sir John Charles, Chief Medical Officer to the Ministry of Health, for his good offices in obtaining some recent unpublished mortality figures; the Registrar-General of England and Wales; the Chief Medical Officer to the Department of Health for Scotland; and all the medical officers of health who supplied me with so much information.

Further, I thank Professor R. S. Illingworth for his criticism; Dr. R. R. Gordon, Dr. J. Kennedy, and Dr. E. G. Herzog for information regarding tuberculous children under their care; Mr. J. F. Scott, M.A., of the Department of Mathematics, University of Sheffield, for his help with the statistics; and Mr. A. S. Foster for the drawing of the chart.

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TUBERCULOUS MENINGITIS TREATED WITH A.C.T.H. AND ISONIAZID

A COMPARISON WITH INTRATHECAL STREPTOMYCIN

BY

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Until the advent of streptomycin, tuberculous meningitis was a fatal disease. With the use of intrathecal streptomycin the mortality was reduced to 40–50% by most workers (Cocchi and Pasquinucci, 1950; Smith and Vollum, 1950; Lincoln and Sifontes, 1953). A change in the intrathecal schedule to daily injections over a very prolonged period and the earlier diagnosis of the disease have reduced the mortality still further (Cocchi and Pasquinucci, 1950; Smith and Vollum, 1950; Lincoln and Sifontes, 1953). Cairns, Smith, and Vollum (1950), whilst experimenting with intrathecal tuberculin, found that this substance, given intrathecally, was able to aid the resorption of the thick basal exudate that is always present in fatal cases, and this, with the concomitant use of intrathecal streptomycin, has salvaged some of the cases that were hitherto considered incurable (Cairns *et al.*, 1950; Smith and Vollum, 1950).

In an attempt to prevent the formation of the thick basal exudate and to control the development of tuberculous endarteritis it was decided to try the effect of intramuscular or subcutaneous adrenocorticotrophic hormone (A.C.T.H.), using isoniazid (isonicotinic acid hydrazide) by mouth also, instead of intrathecal streptomycin. It has been demonstrated that isoniazid given by mouth enters the cerebrospinal fluid (C.S.F.) in high concentration (McDermott, 1952), and it was hoped that by controlling the cellular reaction with A.C.T.H. the tubercle bacilli would be left free for antibiotic attack instead of being enmeshed and inaccessible in the thick basal exudate.

This work was started with children at King George V Hospital, Durban, in March, 1952. In September, 1952, after we had satisfied ourselves of the efficacy of this treatment by treating 13 cases in this way, intramuscular streptomycin and oral *p*-aminosalicylic acid (P.A.S.) were added to the schedule to delay the development of resistant strains of tubercle bacilli. Many of these patients have extensive tuberculosis in other parts of the body.

In 1950 our overall mortality rate from tuberculous meningitis was 60%; this was reduced to 10% in 1951, when earlier diagnosis was made and daily intrathecal streptomycin was given until the C.S.F. was normal for several months.

The mortality rate for the present series is 6.45%; this includes three patients who were having intrathecal streptomycin and who were changed to the new regime (the intrathecal streptomycin being discontinued); also five patients to whom intrathecal streptomycin was also given because of our inexperience with A.C.T.H. and isoniazid at this time, and our fear that the patients might suffer.

Classification of Cases

The streptomycin group (31 cases) and the present series (31 cases), though unselected, are fairly comparable in the numbers of early, intermediate, and late cases. The comparative mortality for the two groups is shown in Table I.

The following criteria have been used as a basis for our classification at time of diagnosis.

Early.—Fever, vomiting, headache, drowsiness, neck stiffness, and/or bulging fontanelle and/or positive Kernig sign in a known tuberculous patient with a raised C.S.F. cell count, protein, and globulin, and a variable chloride and sugar content.

Late.—As above, plus clouding of consciousness or coma, paralysis, and/or multiple fits and grossly abnormal C.S.F. findings.

Intermediate.—Cases lying between the two extremes.

Action of A.C.T.H.

Before the advent of isoniazid A.C.T.H. had been tried experimentally in three children suffering from tuberculous meningitis—two with hemiplegia, and one subject to multiple fits; two of these children were mentally abnormal. There was an obvious improvement in all three. Unfortunately the supply was adequate for only one week's trial. All children had been receiving intrathecal streptomycin for some months.

The action of A.C.T.H. is well demonstrated in the following case history (No. 53, Table III).

A Bantu girl aged 7 years was admitted on December 17, 1952, with tuberculous meningitis. She was emaciated and dehydrated, had a left facial paralysis, was drowsy but could be roused, and was doubly incontinent. She improved rapidly on our new regime, but on February 9, 1953, the C.S.F. was observed to be turbid, though no growth was obtained on culture for secondary organisms. By February 12 it was evident she was developing a partial spinal block, and A.C.T.H. was given again. Table II

TABLE II

Date	Cells per c.mm.	Protein (mg./100 ml.)	Chloride (mg./100 ml.)	Sugar (mg./100 ml.)	Pressure
2/2/53	76	158	—	44	Normal
9/2/53	184	248	640	36	Low
12/2/53 (lumbar fluid)	338	286	680	18	Very low
12/2/53 (cisternal fluid)	48	158	660	33	Raised
16/2/53 (lumbar fluid)	4	57	675	58	Normal

TABLE I

Date	Early			Intermediate			Late			Total Cases
	Cases	Deaths	Cause of Death	Cases	Deaths	Cause of Death	Cases	Deaths	Cause of Death	
1950	0	0	—	4	2	Both from tuberculous meningitis	6	6	4 tuberculous meningitis; 1 cerebral tuberculoma (one year later, meningitis healed); 1 hydrocephalus (one year later, meningitis healed)	31
1951	11	2	1 tuberculous septicaemia; 1 extensive bilateral pulmonary tuberculosis and cerebral tuberculoma and tuberculous meningitis	3	0	—	7	3	1 tuberculous meningitis; 1 lobar pneumonia (meningitis healing); 1 superior sagittal sinus thrombosis (meningitis healing)	
Present series	8	1	1 cor pulmonale (meningitis healing)	6	0	—	17	5	2 tuberculous meningitis; 1 pyogenic meningitis; 1 cerebral tuberculoma and cerebral softening (meningitis healing); 1 cause unknown (meningitis healing)	31

Table III gives a detailed analysis of these cases.

TABLE III.—*Analysis of 62 Cases of Tuberculous Meningitis Treated Since 1950*

Case No.		Age in Years	Pulmonary or Other Tuberculosis	Classification	Treatment	Result	Cause of Death
1	29/3/50	2½	Miliary tuberculosis	Late	1+1A	Death	Tuberculous meningitis
2	6/4/50	3	,, ,,	Intermediate	1+P.P.D.	..	,, ,,
3	5/6/50	10	Bilateral pulmonary tuberculosis	Late	1	,,	,, ,,
4	17/6/50	5	Miliary tuberculosis + cervical adenitis	Intermediate	1+1A	,,	,, ,,
5	22/6/50	2	Miliary tubercu osis	Late	1+1A	,,	,, ,,
6	29/7/50	9/12	,, ,,	,,	1+P.P.D.+1A	,,	Tuberculoma. Meningitis healed
7	11/8/50	5	Miliary tuberculosis + cervical adenitis	Intermediate	1+3 (in 1952)	Recovery—deaf and precocious puberty	—
8	28/10/50	4	Miliary tuberculosis + tuberculous knee-joint	,,	1	Recovery—deaf	—
9	20/11/50	20/12	Progressive primary pulmonary tuberculosis	Late	1+1A+P.P.D.	Death	Hydrocephalus. Meningitis healed
10	27/12/50	2	Miliary tuberculosis	,,	1	,,	Tuberculous meningitis
11	23/1/51	11/12	Primary pulmonary tuberculosis	Early	1+A.C.T.H. 1/52 in Feb., 1952	Recovery, but very retarded	—
12	27/1/51	5	Calcified primary pulmonary. Complex+spinal caries	,,	1	Recovery—deaf	—
13	31/1/51	7	Gross bilateral pulmonary tuberculosis	,,	1	Death	Tuberculoma of brain+tuberculous meningitis+extensive tuberculosis
14	25/2/51	7/12	Primary pulmonary tuberculosis	,,	1	Recovery	—
15	4/3/51	12	Calcified primary pulmonary. Complex+spinal caries	Intermediate	1	Recovery—deaf	—
16	4/3/51	6	Progressive primary pulmonary. Tuberculosis + spinal caries with paraplegia	Late	1	,, ,,	—
17	6/4/51	1	Miliary tuberculosis	,,	1+1A+P.P.D.+2	Recovery—deaf, blind, hydrocephalic, and quadriplegic	—
18	11/4/51	10/12	Miliary tuberculosis+unilateral pulmonary cavitation	,,	1	Death	Superior sagittal sinus thrombosis, meningitis resolving
19	10/5/51	3	Miliary tuberculosis	,,	1	,,	Tuberculous meningitis
20	11/5/51	15/12	,, ,,	Early	1	Recovery	—
21	13/7/51	4	Progressive primary pulmonary tuberculosis	,,	1	,,	—
22	14/7/51	3	Primary pulmonary tuberculosis	Late	1+1A+P.P.D.+2 A.C.T.H. 1/52 in Feb., 1952	Death	Pneumonia. Meningitis resolving
23	31/8/51	8	Pleural effusion	Early	1	Recovery—deaf	—
24	20/9/51	13	Miliary tuberculosis + tuberculous septicaemia	,,	1+2	Death	Jaundice and anaemia
25	26/10/51	5	Miliary tuberculosis+spinal caries	,,	1	Recovery—deaf	—
26	7/11/51	4	Progressive primary pulmonary tuberculosis+cervical adenitis. Spinal caries developed under treatment	Late	1+A.C.T.H. 1/52 in Feb., 1952	,, ,,	—
			C.S.F. relapse after 10 months		4	Rapid response	—
27	10/12/51	5	Miliary tuberculosis	Early	1	Recovery	—
28	14/12/51	7	Progressive primary pulmonary tuberculosis	Intermediate	1	,,	—
29	20/12/51	9/12	Primary tuberculosis	Late	1	,,	—
30	31/12/51	Adult	Miliary tuberculosis	Intermediate	1+decompression of right lateral ventricle for sudden hemiplegia	Recovery—deaf	—
31	7/1/52	5	Bilateral pulmonary tuberculosis	Early	1	Recovery	—
32	7/2/52	3	Miliary tuberculosis	,,	1 for 3/52 then isoniazid alone	,,	—
33	7/3/52	2	,, ,,	Late	1+isoniazid	Recovery after partial spinal block	—
34	29/3/52	18/12	Primary pulmonary tuberculosis	Early	3+isoniazid alone for C.S.F. relapse	Recovery	—
35	1/4/52	5	Miliary tuberculosis + spinal caries	Intermediate	3	,,	—
36	9/4/52	10	Bilateral pulmonary tuberculosis + calcified tuberculoma of brain	Early	3	,,	—
37	30/4/52	3	Miliary tuberculosis	,,	1→3	,,	—
38	11/5/52	5	Primary pulmonary tuberculosis	Late	3	Death	Cause unknown. Meningitis resolving
39	6/6/52	14/12	Miliary tuberculosis	,,	3+1	Death in 1 week	Tuberculous meningitis+disseminated tuberculosis
40	6/6/52	8	Primary pulmonary tuberculosis +spinal caries	Early	3	Recovery	—
41	14/6/52	2½	Primary pulmonary tuberculosis	Late	3+1	Death	Pyogenic meningitis
42	18/6/52	5½	Primary pulmonary tuberculosis +cervical adenitis	,,	3+1	Recovery after coma lasting 5 weeks	—
43	23/6/52	6	Progressive primary pulmonary tuberculosis+cervical adenitis	Intermediate	3	Recovery	—
44	25/6/52	2½	Miliary tuberculosis	Late	3+1+tryptar	Recovery after spina block	—
45	11/7/52	18/12	,, ,,	,,	3	Recovery	—
46	22/8/52	2	Bilateral pulmonary tuberculosis	Early	4	Death	Cor pulmonale
47	8/9/52	3	Miliary tuberculosis	Late	4	,,	Tuberculoma of brain, cerebral softening, meningitis resolving
48	12/9/52	10	,, ,,	,,	4	Recovery	—
49	24/9/52	2	Progressive primary pulmonary tuberculosis+spinal caries	,,	4	Death	Spinal caries with exposure of dura and tuberculous meningitis
50	14/10/52	16	Primary pulmonary tuberculosis	,,	4→1→(1+4)	Admitted with paraplegia and retention of urine. Making slow progress. Deaf. Isoniazid omitted temporarily because of mental derangement	—
51	22/11/52	6	Healed miliary tuberculosis+active spinal caries	Intermediate	4	Recovering	—
52	26/11/52	6	Miliary tuberculosis	Late	4+2 extra courses A.C.T.H.	Recovering (see text)	—
53	17/12/52	7	Bilateral pulmonary tuberculosis	,,	4+1 extra course A.C.T.H.	,, ,, ,,	—

TABLE III.—*Analysis of 62 Cases of Tuberculous Meningitis Treated Since 1950.* (Continued.)

Case No.		Age in Years	Pulmonary or Other Tuberculosis	Classification	Treatment	Result	Cause of Death
54	20/12/52	2½	Bilateral pulmonary tuberculosis +spinal caries	Early	4	Recovering	—
55	20/1/53	1	Primary pulmonary tuberculosis	Late	4	,,	—
56	21/1/53	7	Miliary tuberculosis	Intermediate	4	,,	—
57	26/1/53	15/12	,, ,,	Late	4	Recovering. Hemiplegic still	—
58	28/1/53	4	Miliary tuberculosis + spinal caries	Early	4	Recovery	—
59	12/2/53	10	Miliary tuberculosis	Late	4	Recovering after spinal block	—
60	3/3/53	21/12	,, ,,	,,	4	Rapid deterioration, followed by slight improvement	—
61	24/3/53	9	Unilateral pulmonary cavitation	Intermediate	4	Recovering	—
62	27/3/53	22	Abdominal tuberculosis	,,	4	,,	—

1=Intrathecal streptomycin+intramuscular streptomycin (I.M.S.)+oral P.A.S. 1A=Intraventricular therapy. 2=Intravenous P.A.S. 3=A.C.T.H.+isoniazid. 4=A.C.T.H.+isoniazid+I.M.S.+oral P.A.S. Recovering=C.S.F. almost normal and patient apparently normal.

demonstrates its effectiveness. After this the fluid gradually returned to its previous state and has progressively improved.

Post-mortem examinations performed on patients with tuberculous meningitis who were treated with this regime, and who died of extensive tuberculosis in other organs or of other diseases, have not shown such gross basal exudate as we were accustomed to seeing, and some presented a "clean brain."

Scheme of Treatment

1. A.C.T.H., 6 to 25 I.U. six-hourly intramuscularly or 12 to 50 I.U. twice a day of the gel subcutaneously; this is given for one week if the patient makes steady progress. It is continued longer if the response is not as good as expected or if there is a block, partial or complete. A patient admitted in coma is usually able to answer questions and help to feed himself by the end of a week. It has been given for as long as five weeks, with no toxic effects or withdrawal symptoms, other than moon-face and some oedema.

2. Isoniazid is given by mouth in dosage of 4 mg. per lb. body weight per 24 hours, but the first two doses are equivalent to 8 mg. per lb.; the dose is increased as the weight increases, and very thin children are given the dose for their expected weight. Intramuscular isoniazid has been used, but does not seem any more effective, though it is of use in patients who are vomiting. Intrathecal isoniazid has also been tried and found to be both irritant and unnecessary, and, as this drug has no antibiotic action against the usual secondary organisms, the risk of a secondary septic meningitis is very great.

3. Streptomycin, 0.02 g. per lb. body weight per 24 hours to the nearest 0.5 g., but not exceeding 1 g., is given daily until the temperature settles and improvement is assured, and then every third day.

4. P.A.S., 0.1–0.15 g. per lb. body weight per 24 hours by mouth.

5. C.S.F. is collected weekly for examination—bi-weekly for the first two to three weeks.

Cerebrospinal Fluid Findings

Whilst A.C.T.H. is administered there is a marked fall in cells and protein in the C.S.F.; on discontinuing the drug the cells rise slightly, and the protein more so; this rise continues for a few weeks, and then there is a gradual fall until the whole C.S.F. picture returns to normal. The C.S.F. appears to return to normal more quickly than in the streptomycin-treated cases—that is, in one to four months.

Complications.—Complications which have been observed are (1) moon-face; (2) oedema; (3) septic complications—(*a*) pyogenic meningitis (Case 41); (*b*) acute otitis media (Case 55); (4) mental disturbances due to isoniazid in one adult patient.

Discussion

This form of treatment is simple to administer, but the A.C.T.H. or isoniazid can easily be forgotten. It is a maxim in dealing with tuberculous meningitis that the disease and its complications must be treated early and adequately. A good deal of experience with cases of tuberculous meningitis is necessary when using this regime. Without daily lumbar punctures (as with intrathecal streptomycin therapy) one does not automatically inspect the C.S.F. daily for change in colour and turbidity or observe pressure changes. One must rely on one's clinical judgment to determine if additional punctures—lumbar, cisternal, or even ventricular—are necessary to control raised intracranial pressures or to diagnose complications. This is shown by the following case (No. 52, Table III).

An Indian girl aged 6 years was admitted in coma on November 26, 1952; she could be roused, but resented disturbance, and one could not communicate with her. She made a fair initial improvement, but on December 4, after the A.C.T.H. was discontinued, she relapsed slightly, and the lumbar C.S.F. pressure was very low; this necessitated an immediate cisternal puncture to eliminate the possibility of a spinal block. She later developed a left hemiparesis, and the A.C.T.H. was recommenced. On December 30 the C.S.F. was completely normal, and remained so for one week, but the child was very restless and had difficulty in swallowing.

On January 3, 1953, she became worse, possibly owing to toxicity of A.C.T.H. and/or isoniazid, but both these were discontinued without improvement until January 8, when isoniazid was again given. On January 7 she did not swallow, but either held the food in her mouth or let it run out. Bilateral prefrontal burr-holes were made and the lateral ventricles explored, but very little fluid was obtained. There was, however, a transient improvement. She soon relapsed and required tube feeding. On January 19 she could be fed by mouth again with very great difficulty. On January 28 she was becoming very noisy; the C.S.F. was only slightly abnormal, but sedatives and forced feeding were still necessary. On February 26 the C.S.F. pressure was raised and the fluid was markedly abnormal. A.C.T.H. was re-administered for three weeks with dramatic improvement, and by April 7 she was able to sit up, help to feed herself, laugh, and talk. She would sing an Indian song on request, and she also spoke in English. On May 21 she stood up alone for the first time.

Conclusion

The form of therapy described above is producing very gratifying results, and there have been no cases of deafness, and no clinical or radiological evidences of spread of pulmonary tuberculosis whilst A.C.T.H. was being administered.

As most of our patients are small children the avoidance of the ordeal and danger of the daily lumbar puncture is a great advance. Intrathecal streptomycin is now a thing of the past in this hospital.

I wish to thank Dr. B. A. Dormer, medical superintendent, King George V Hospital, Durban, for his help and encouragement in carrying out this work.

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TREATMENT OF TUBERCULOUS MENINGITIS

BY

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The appearance of the article by Russell and MacArthur (1953) on the treatment of tuberculous meningitis with intrathecal streptomycin, and the results reported therein, prompts one to wonder whether this is a very good method of treatment. As so often in the past, one wonders how many of the after-effects are due to the disease and how many to the treatment. Clark, Elmendorf, Cawthon, Muschenheim, and McDermott (1952) have reported the use of isoniazid in the treatment of miliary and meningeal tuberculosis. They expressed the hope that the use of isoniazid orally and streptomycin by the intramuscular route might permit the elimination of the intrathecal use of streptomycin without sacrificing the maximal obtainable antimicrobic activity within the central nervous system. A similar hope led to the use of this regime in three cases of tuberculous meningitis. Although it is obviously too early for final assessment, it is felt that the quite remarkable improvement obtained and maintained should be reported even at the risk of prematurity.

Case 1

A coloured female child aged 3 was admitted on March 12, 1952. On January 1 a diagnosis of tuberculous meningitis had been made and proved elsewhere. Initially intramuscular and intrathecal streptomycin were given for 49 days. A right sixth-nerve paralysis was noted and her general condition was described as apathetic and listless. As she did not respond to this therapy, increasing doses of intrathecal purified protein derivative were given in addition to streptomycin, with some slight improvement. She received 50 mg. of streptomycin and 5 μg. of purified protein derivative every other day intrathecally, together with 1 g. of streptomycin intramuscularly daily. Her cell count varied between 280 and 350 per c.mm. At the time of her admission to this hospital she was found to be apathetic and almost completely blind. She had paralysis of the sixth nerve on the right and a probable defect in associated ocular movement. The optic disk showed evidence of early primary optic atrophy. A spastic paralysis on the right and a flaccid paralysis on the left affected the lower limbs almost entirely. There was paralysis of the left sternomastoid muscle. She was incontinent of urine and faeces. Examination of the spinal fluid showed 366 cells per c.mm. and a total protein of 230 mg. per 100 ml. Intrathecal therapy was continued, but her general condition did not improve. The cell count rose to 490 per c.mm.

On April 1 it was decided to discontinue intrathecal therapy, to persevere with the intramuscular streptomycin and oral P.A.S., and to give, in addition, 50 mg. of isonicotinic acid daily. The improvement was remarkable. Two weeks after discontinuation of the intrathecal therapy the cell count of the cerebrospinal fluid was 88 per c.mm. and the protein estimation was 75 mg. per 100 ml. One month after starting isoniazid therapy the child was up in a wheelchair. After a further two weeks the cell count was 9 per c.mm., all lymphocytes. On July 16 her sight was regarded as normal. There was no paralysis and her gait was good. At the time of writing, one year after the commencement of isoniazid therapy, she was a normal child.

Case 2

A coloured woman aged 23 was admitted on November 18, 1952. Ten weeks previously the diagnosis of tuberculous meningitis had been proved and treatment instituted elsewhere. Her treatment consisted of daily intrathecal and intramuscular streptomycin together with P.A.S. A flaccid paralysis of the lower extremities appeared and showed no signs of improvement. At the time of her admission to this hospital she was found to be well developed. She was having some difficulty with speech and was slightly disorientated. The abdominal muscles showed spasm and tenderness, with hyperactivity of the abdominal reflexes. The upper extremities were grossly normal. The lower extremities showed an extensive flaccid paralysis with hyperaesthesia. Examination of the cerebrospinal fluid showed 348 cells per c.mm. (96% lymphocytes, 4% polymorphs).

In the light of the previous case and with the knowledge that intrathecal therapy had not already effected any great improvement, it was decided to give the patient no further intrathecal medication, but to rely on intramuscular streptomycin, 1 g. twice a week, P.A.S., 12 g. daily by mouth, and 6 mg. of isonicotinic acid derivate per kg. daily. Within two weeks her condition had greatly improved both objectively and subjectively. She became completely orientated and had no complaints. Her legs were no longer painful, and they increased in strength daily. Three weeks after the beginning of the treatment the cell count was 88 per c.mm. Two months later it was 2 per c.mm. At this date examination rated all the leg and abdominal muscles as either good or normal. In March, 1953, a cerebrospinal fluid examination showed a normal cell count, there was normal power in the lower extremities, and she was asymptomatic.

Case 3

A white male aged 30, with a long history of extrapulmonary tuberculosis involving the spine and the sternum, was operated on for fusion of the spine from D 10 to L 1 on July 3, 1952. The post-operative course was uneventful and progress to fusion steady. In December he became fully active wearing a brace, and was asymptomatic. On January 5, 1953, he first developed extremely severe headaches. Lumbar puncture was done and fluid was found to be under a presssure of 200 mg. of water. A cell count showed 239 cells (98% lymphocytes); total protein was 55 mg. per 100 ml. The cerebrospinal fluid was negative for tuberculosis by guinea-pig test and by culture, but the tuberculous nature of the meningitis was assumed. The patient had been under treatment with streptomycin intramuscularly and P.A.S. orally for one year until December 23, 1952.

X-ray examination showed disease well below the spinal fusion. The fusion was solid from the tenth dorsal vertebra to the first lumbar. The second lumbar vertebral body was diseased, with thinning of the intervertebral disk between the second and third lumbar vertebrae. Streptomycin intramuscularly, 1 g. three times a week, P.A.S., 12 g. daily, and ditubin, 400 mg. daily, were started on January 5, 1953. Two weeks later the patient was virtually asymptomatic and the cell count had fallen to 16 per c.mm. The total protein was 30 mg. per 100 ml. At the time of writing, three months after his acute episode, he was completely asymptomatic.

Conclusion

These three cases are obviously too few in number and of too limited duration to be the subject of dogmatism. However, they do indicate that intrathecal streptomycin is potentially dangerous and is apparently no more beneficial than the combination of intramuscular streptomycin and oral isonicotinic hydrazide and P.A.S. No trial has been made of isonicotinic hydrazide alone, as most workers have felt that the optimum effect is obtained by using all three drugs. Further findings will be reported when a greater number of cases have been treated for a longer period.

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PORPHYRIA CUTANEA TARDA IN RELAPSE: A CASE REPORT

BY

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The relative frequency of the various types of porphyria (Waldenström, 1937; Watson, 1951) is calculable only from observation upon large series. Watson and colleagues (1951), reporting 88 cases of porphyria, observed over a 14-year period, found only 5 patients with congenital porphyria, 10 with "mixed" (cutanea tarda) porphyria, and 73 with acute porphyria. Nevertheless, porphyria cutanea tarda may be much more common than is supposed (Macgregor, Nicholas, and Rimington, 1952; Wells and Rimington, 1953), since "attacks" or exacerbations may closely simulate those of acute porphyria; unless a stool porphyrin determination is carried out during remission, a distinction is at times hardly possible. The finding of normal urinary porphyrin in a patient seen only in the remission phase might lead to the exclusion altogether of porphyria from the diagnosis, but a stool porphyrin determination will always reveal the excessive total porphyrin excretion. Increased vigilance in dermatological case material might be rewarding. Brunsting and associates (1951) referred to 21 cases of the adult form of chronic porphyria with cutaneous manifestations seen at the Mayo Clinic in the previous six years.

The case described below was first seen during the course of an attack, and only on one day were porphobilinogen and uroporphyrin present in the urine, although both coproporphyrin and protoporphyrin were regularly present in considerable amount. As the attack subsided, the faecal porphyrin rose and urinary porphyrin diminished.

Case Report

A mechanic aged 26 was admitted as a surgical case to Whipps Cross Hospital on March 12, 1952. His chief complaints were central abdominal colic, frequent vomiting, and inability to pass faeces or flatus for three days. He had a generalized exudative skin eruption of three weeks' duration, following on crops of vesicles one month previously. There had been three similar episodes of vesication in the previous two years. Vesicles cleared within a fortnight on two of these occasions. On the third, which occurred one week after the injection of varicose veins with "ethamolin" (5% ethanolamine oleate, *B.P.*, in 2% benzyl alcohol), he was admitted to a dermatological unit and was discharged a fortnight later with a diagnosis of sensitization dermatitis. He had taken no barbiturate drugs during or immediately before this incident. No relative had suffered from vesication similar to that of our patient so far as inquiry indicated. Neither the patient nor his parents could recall having passed dark or red urine. The patient stated that he was a strict total abstainer from alcohol.

Physical examination revealed a robust and plethoric man, who stated that he had recently weighed 14 stone (88.9 kg.). Small weeping lesions were observed on his forehead. His "rosy apple" complexion was partly due to telangiectatic vessels. These bore no resemblance to the angiomatous lesions of Osler's disease or to spider naevi. The knees were constantly flexed. Physical signs, apart from skin manifestations, were confined mainly to the abdomen, which appeared somewhat distended, but moved with respiration. The percussion note was resonant throughout, but bowel sounds were absent and no peristalsis was observed. Neither rebound tenderness nor palpable masses were found. The hernial orifices were clear and rectal examination was negative. There was an intense desire to pass flatus, but inability to do so.

Violaceous areas were noticed on the lower outer aspects of the legs, while scattered weeping lesions were observed on the upper limbs and trunk. Mottled palmar erythema and a few small scars were seen on the hands. Temperature and routine urinary analysis were normal; the blood pressure was 115/80. A provisional diagnosis of subacute obstruction of the small intestine was made. A straight *x*-ray film of the abdomen partly supported this diagnosis by revealing gaseous distension, but without actual fluid levels. Agonizing abdominal colic persisted, and on the following day (March 13) laparotomy was performed, but there was no demonstrable lesion.

Progress

On March 16 the patient developed a psychosis with confusional, depressive, hysterical, and paranoid features, lasting one week. The urine, which previously was orange-coloured, now had a burgundy hue. A clinical diagnosis of porphyria was made, and was confirmed chemically. The urine showed red fluorescence in ultra-violet light, while the Watson–Schwartz test for porphobilinogen was positive. On March 17 pentobarbitone sodium, 3 gr. (0.2 g.) nocte, was given. On the 18th a right-sided facial paresis appeared, without other neurological signs. The bowels were opened and he passed flatus. The skin lesions had now almost disappeared. Next day phenobarbitone, 1 gr. (65 mg.), was given, but on March 20 all barbiturates were prohibited. On the 25th a flaccid quadriplegia with urinary incontinence was present.

By March 27, although orientated and rational, he was apathetic and readily lost the power of concentration. He had a bilateral partial ptosis, but the right-sided facial weakness was now scarcely demonstrable. The pupils were large, equal, and reacted slowly to light. Eye movements were full and there was neither nystagmus nor diplopia. The fundi and visual fields were normal. The corneal reflexes were sluggish, but the pharyngeal reflex was brisk. There were neither meningeal nor bulbar signs.

The remaining signs were confined to the limbs, where gross weakness without fasciculation was demonstrable, especially in the girdle regions. Limb reflexes were absent apart from a minimal response in the ankle-jerks. The plantar responses were flexor. Sensory loss was restricted to the upper limbs, where he was unable to discriminate between a sharp prick and blunt pressure.

A tachycardia (118 a minute) and a moderate hypotension (95/75) occurred. The abdominal colic, although controlled by pethidine (100 mg. intramuscularly), recurred during the next three weeks. The sensory loss and ptosis disappeared after three days, but recovery from the quadriplegia was so gradual that even at the end of six months he was only just able to walk unaided.

Six weeks after admission two fresh signs involving the appendages and skin were apparent. These were the presence of Beau's lines on the nails, producing a transverse groove just distal to the lunula, and the development of a melanosis of the forehead, neck, and extensor surfaces of the forearms. The latter cleared over the next four months.

Investigations

Serial values for blood counts, serum electrolytes, and hepatic tests are indicated in Table I. There was pronounced elevation of the first blood urea result and of the first two leucocyte counts. This leucocytosis could be partly attributed to the development of suppuration at the site of

TABLE I.—*Blood Chemistry and Liver-function Tests*

	March 18–24	March 28–31	April 18–22	July 14–24	October 24–31
Haemoglobin %	94	94	92	108	
W.B.C./c.mm.	27,800	26,400	13,600	3,600	5,000
Blood urea (mg./100 ml.)	102	32	45	25	—
Serum proteins (g.%)	5·6	5·0	6·4	6·3	7·1
Albumin (g.%)	3·5	3·4	3·1	3·7	4·1
Globulin (g.%)	2·1	1·6	3·3	2·6	3·0
Serum bilirubin (mg./100 ml.)	1·4	0·5	0·5	—	—
Thymol turbidity (units)	1	1	2	—	—
Serum alkaline phosphatase (K.-A. units)	5	—	5	4·5	—
Prothrombin index (%)	74	—	100	—	—
Serum cholinesterase (μl. CO_2/ml./10 min.)*	—	—	40·81	59·88	—
Bromsulphthalein (% retention)	—	—	42	7	—
Schlesinger test on urine	Pos.	Pos	Neg.	Neg.	Neg.
Serum sodium (mg./100 ml.)	—	280	285	295	330
Serum chloride (mg./100 ml., as NaCl)	—	510	521	545	560
Serum potassium (mg./100 ml.)	—	20	16	18	20

* Lower limit of normal = 30.

the abdominal wound. Some impairment of liver function was evident (serum proteins, cholinesterase activity, prothrombin index, also bromsulphthalein retention, serum bilirubin, and urinary urobilin). No associated proteinuria was demonstrable. Electrophoresis of plasma proteins (April 20) revealed no gross alteration from the normal ratio. The E.S.R. was normal. The plasma pyruvic acid level (March 20) was 0.8 mg. per 100 ml., a value within normal limits. The Wassermann reaction was negative.

Electrolyte metabolism was also deranged. Thus prolonged low levels of serum sodium and chloride were observed. Serum potassium values remained within normal limits. No abnormality in adrenal function was demonstrable. The Kepler water-diuresis test yielded normal results (April 19 and July 23), while the Thorn test (April 9) showed an adequate eosinopenic response.

A limited investigation of renal function was carried out. In the first week in hospital, two catheter specimens of urine showed no microscopical abnormality. The urea concentration and urea clearance tests gave normal results, but were not conducted until four months after his admission.

A plain *x*-ray film of the abdomen (March 17) revealed gaseous distension. A barium meal with follow-through studies (May 19) showed dilatation of the terminal ileum with segmentation of the barium. The time taken for the barium to pass through the intestines was within normal limits.

Electromyography (May 8) showed no nerve conduction from the left brachial plexus when this was stimulated over Erb's point. On exploration of the left deltoid and biceps the motor activity on volition was grossly decreased to the point of being discrete, while fibrillation was present at rest. The results suggested gross denervation of the type found in polyneuritis.

Exposure to ultra-violet light and to the carbon arc lamp (April 4) was conducted when his abdominal colic appeared to have subsided. The volar surface of the left forearm was exposed to the ultra-violet lamp for periods of one-half, one, and one and a half minutes without producing any local reaction in the next two days. The back of the left forearm was exposed to the carbon arc lamp for four minutes without local reaction, but after the first three minutes he complained of a recurrence of colic. This was so severe that he could not speak, but it lasted only a few hours.

Skin biopsy (September 8) of the right forearm over a melanotic area showed atrophic skin with no dermal papillae, and there was dense melanin pigmentation of the basal layer. Iron was present and mucoid material was demonstrable in the corium.

Serial electrocardiograms were normal.

Porphyrin Determinations.—The serum showed a red fluorescence to ultra-violet light on March 25, regressing to a faint but definite fluorescence three days later. The urine was analysed on six occasions between March 25 and April 6. Porphobilinogen was present on the first occasion only. Stool porphyrins were determined on April 6, and again on April 22 and July 5. The results of these investigations are recorded in Table II, together with a follow-up in March, 1953.

The stool of July 5 contained the large amount of 2 mg./g. dry weight of porphyrin (upper normal limit, 30 μg./g. dry weight) at a time when the urine contained only 0.73 mg./l. total porphyrin. This relationship is characteristic of porphyria cutanea tarda in remission.

TABLE II.—*Porphyrin Content of Urine and Stool Specimens*

Date	Uro-porphyrin	Copro-porphyrin	Proto-porphyrin	Porpho-bilinogen
Urine				
25/3/52	8·3 mg./24 hr.	4·7 mg./24 hr.		+
27/3/52	Nil	1·1 ,, ,,	1·9 mg./24 hr.	−
28/3/52	,,	1·1 ,, ,,	4·0 ,, ,,	−
31/3/52	,,	1·0 mg./l.	0·4 mg./l.	−
2/4/52	,,	1·04 ,,	1·65 ,,	−
6/4/52	,,	1·1 ,,	1·9 ,,	−
5/7/52	,,	(Combined) 0·73 mg./l.		−
15/3/53	,,	(,,) 0·39 ,,		−
Stool				
6/4/52	,,	0·56 mg./g. dry wt.	0·37 mg./g. dry wt.	
22/4/52	,,	0·26 ,, ,, ,,	0·37 ,, ,, ,,	
5/7/52	,,	0·76 ,, ,, ,,	1·30 ,, ,, ,,	
15/5/53	,,	0·34 ,, ,, ,,	0·41 ,, ,, ,,	

Discussion

Porphyria cutanea tarda is the term reserved for cases with late appearance of the skin manifestations which are the usual presenting symptoms. It is a fairly benign condition when the hydroa vacciniforme lesions alone are present. It predominates slightly in males and is usually observed in the third to fifth decades. The salient clinical features are : vesicular and erosive skin lesions, particularly on the backs of the hands and especially following exposure to heat, light, or trauma ; a violaceous complexion, often with suffused sclerae ; a tendency to melanotic and sclerodermatous changes ; and, occasionally, hypertrichosis. Waldenström (1937) referred, in his original description of this form of porphyria, to the absence of abdominal and nervous symptoms. Later study of the disease has, however, revealed that attacks or exacerbations may occur during which abdominal colic may be mild to severe and paralyses may even be seen (Brunsting *et al.*, 1951 ; Macgregor *et al.*, 1952).

Porphobilinogen may make its appearance for a few days at the height of the attack, but the quantity is never great and it may even be absent altogether. Urinary porphyrin is generally increased in this disease, but its type is variable. Some patients with marked cutaneous lesions excrete uroporphyrin regularly, and the series I isomer appears to predominate (Canivet and Rimington, 1953) ; others excrete uroporphyrin (of variable isomer composition) during attacks, together with coproporphyrin and protoporphyrin, while yet others have a normal urinary porphyrin during remission but excrete substantial amounts of coproporphyrin and protoporphyrin during exacerbations. It is indeed difficult to decide whether such different cases illustrate phases in the progression of the disease or whether further subdivision is required into distinct pathological entities. This question can best be answered by watching the progress of known cases and avoiding hasty generalizations. There is, however, one feature common to cases of porphyria cutanea tarda which serves to distinguish them from cases of acute porphyria—namely, the observation that in porphyria cutanea tarda during remission faecal porphyrin is raised much above normal. During attacks it falls as the urinary porphyrin rises, the plasma evinces red fluorescence, and the serum bilirubin is generally raised (Gray, Rimington, and Thomson, 1948 ; Macgregor, *et al.*, 1952 ; Wells and Rimington, 1953).

There is ample clinical and biochemical evidence to support a diagnosis of porphyria cutanea tarda in our patient. The onset with vesicular eruptions is characteristic; however, a diagnosis of acute porphyria would have been difficult to refute in their absence, since the episode of abdominal colic was accompanied in his case by fairly severe involvement of the nervous system, giving a clinical picture closely simulating acute porphyria in relapse.

While the cause of the present attack remains obscure one of the previous attacks was probably precipitated by an injection of the sclerosing agent "ethamolin" into a varicose vein. Apparently this substance has not been previously suggested as a precipitating cause of attacks of porphyria.

Attention has recently been focused on adrenal and hepatic function in porphyria. Linder (1947) thought that the hypochloraemia sometimes found in acute porphyria could not be due to vomiting, since alkalosis is not present; besides, there is usually a co-existent hyponatraemia. In our patient the low values for serum sodium and chloride persisted for several weeks. Although other workers (Abrahams, Gavey, and Maclagan, 1947) have shared the view that an adrenal cause for this is operative, evidence for a renal cause has also been afforded (Prunty, 1949). In this patient the results of tests do not suggest impaired adrenal function, which, if present, would have an obvious bearing on therapy. It may be noted that both Linder (1947) and Abrahams *et al.* (1947) produced only temporary success by the administration of salt and adrenocortical extract, while trials of A.C.T.H. or cortisone have been negative or at best inconclusive (Oltman and Friedman, 1951; Myerson, 1951; Gilbert, Toupin, and Bell, 1951; Meyers and Griffith, 1952; Goldberg, MacDonald, and Rimington, 1952; Watson, 1952).

Both Davies (1949) and Prunty (1949) consider that a renal rather than adrenal disorder is responsible for the changes in renal tubular function. In our patient, frequent urinalysis and two microscopical examinations of the urine at the height of the illness revealed no abnormality. The blood-urea level, although considerably raised in the first few days after admission, was subsequently within normal limits. The earlier raised value, taken in conjunction with his hypotension and low serum sodium and chloride, suggested that he was then dehydrated, perhaps on account of the post-operative state (Moore and Ball, 1952) and a scanty food and fluid intake at this time.

Frequent reference has been made to impaired hepatic function in porphyria of the acute and cutanea tarda varieties. The results reported here support this view. This subject has been discussed recently by Watson (1952), who has introduced the term "porphyria hepatica" (Watson, 1951) to designate these two types of porphyria where the liver is thought to be mainly responsible for the abnormal porphyrin production, the liver often containing large amounts of porphyrins while values in bone marrow were normal. This situation is reversed in congenital porphyria, which Watson (1951) prefers to call "porphyria erythropoietica."

The radiological signs in cases of porphyria with intestinal colic are well recognized (Mason, Courville and Ziskind, 1933; Nesbitt, 1944; Fisher and Stanley, 1951; Calvy and Dundon, 1952). They consist of segmental gaseous dilatation proximal to the sites of spasm. In the present case barium study revealed segmental dilatation of the intestine, especially involving the caecum.

Electromyographic investigations in paralysis due to porphyria have hitherto received little attention (Massachusetts General Hospital Case Records, 1947; Peters, 1949). The tracings from the present case showed the gross denervation of typical polyneuritis. This was accompanied clinically by acute muscle atrophy as previously described in the case of DiFiore (1946).

The skin biopsy revealed atrophic changes and heavy melanin deposition, as often observed in these cases. The melanosis appeared about six weeks after admission, but had regressed again after a further four months. It involved mainly the upper part of the body, and was well marked in the neck, where it simulated a smear of coal dust. In view of the constipation for the first few weeks after admission, it was wondered whether an associated absorption and skin deposition of indican might explain this pigmentation, but frequent urinary studies failed to show any pathological output of indican, employing the usual reagents of Jaffe, Jolles, and Obermeyer.

The reciprocal urinary/faecal level of porphyrin excretion, previously referred to, was used as an index of commencing remission, and its presence in this case is further confirmation of its occurrence in patients with porphyria cutanea tarda.

Only conservative treatment was adopted, with vitamin-B-group supplements. Pethidine was found to be a reliable antispasmodic to control the colic. Other workers have shown that neostigmine (Waldenström, 1944; Opsahl, 1947; Gordin, 1948; Veflingstad, 1949; Öigaard and Roos, 1953) and the ganglion-blocking agent T.E.A.C. (Wehrmacher, 1952) may be useful alternatives. The role of cortisone and A.C.T.H. awaits further evaluation, according to available reports. Watson (1952) refers to remission within 48 hours in three of six cases treated with cortisone or A.C.T.H., but it is not clear to what extent the result was due to the drugs. Other workers have not found any striking alteration of porphyrin excretion in further single cases so treated.

Physiotherapy was beneficial in encouraging recovery of muscle function in our patient, especially when he was bedridden with paralysis. He returned to light work six months after his admission. By a further three months he had regained his usual weight, which had shown a maximal loss of 3 stone (19 kg.) about four months after admission. Since discharge from hospital he has enjoyed good health, but has been handicapped by residual muscle weakness.

Summary

Investigation is reported of a case of porphyria cutanea tarda in relapse in which severe colic and neurological disturbances were present in addition to cutaneous manifestations. Porphobilinogen and uroporphyrin were detected in the urine on only one occasion; later, only coproporphyrin and protoporphyrin were present, and as the level of these declined that of the faecal porphyrin rose. Electromyography indicated gross denervation of the type found in polyneuritis. The patient still had residual muscle weakness about one year after his attack.

The relation of porphyria cutanea tarda to acute porphyria and congenital porphyria is discussed, and the origin and treatment of symptoms are briefly considered.

We are indebted to Mr. Lang Stevenson and Dr. Eric Smith for permission to investigate this case. Thanks are also due to Professor Nicholas Martin for electrophoretic study of plasma proteins, to Dr. F. Hobbiger for the cholinesterase determinations, to Dr. William Walther for co-operation in the biochemical determinations, and to Drs. P. Bauwens and A. T. Richardson for the electromyographic investigations. To Drs. A. Stein and P. Blaxland we owe thanks for the report on the surgical aspect of the patient. Dr. C. Raeburn carried out the histological studies. Mr. F. Grover gave valuable technical assistance throughout. One of us (C. R.) wishes to thank the Nuffield Foundation for a grant which has made possible the establishment of a unit for the investigation of pyrrole pigment metabolism.

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CUTANEOUS MANIFESTATIONS OF PORPHYRIA

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Cutaneous and Visceral Porphyrias

The porphyrinopathies, diseases in which excessive quantities of a porphyrin or its precursor are excreted in the urine, have a protean symptomatology. The visceral symptoms are now well known, but the cutaneous symptoms are less well understood. Basically, the skin may react in three ways—by vesication, by pigmentation, or by the development of hirsuties.

Vesication usually occurs in spring or summer, when bullae from 1 to 4 cm. in diameter appear on face, hands, forearms, legs, ears, neck, or other exposed areas either as a result of solar irradiation or following slight trauma. The bullae rupture, and heal with scarring, usually mild. If infection occurs granulation tissue is found at the base of the bulla with fibrosis and more severe scarring. "Sclerodermatous" thickening of the skin may result; if the conjunctivae are involved the two layers may fuse. Pigmentation also appears on exposed areas, usually, but not always, after blistering, so that a diagnosis of pellagra (which itself is accompanied by a symptomatic porphyrinuria) is entertained. Hirsuties is uncommon, and usually moderate.

Patients with such skin lesions may be labelled as cases of pemphigus, epidermolysis bullosa, hydroa bullosa, hydroa vacciniforme, eczema solare, lupus erythematosus, erythema exudativum multiforme, summer prurigo, pellagra, or light dermatitis, unless or until the porphyrinuria is discovered. Zeligman and Baum (1948) used the term "porphyric bullous dermatosis" for any combination of these syndromes in a subject found to have a porphyria, while they used the term "epidermolysis bullosa" when blisters developed on exposed areas after slight trauma, and "hydroa aestivale" when blisters developed one to three days after solar irradiation insufficient to cause more than slight inconvenience to a normal subject.

Most workers (Rimington, 1952) agree that true porphyrias are characterized by excretion of uroporphyrin or a precursor, and can be classified into an acute form with colic, constipation, and paralysis, a congenital form with photosensitivity from birth, and porphyria cutanea tarda, in which a bullous dermatosis appears in adult life. We recently studied a patient with porphyria cutanea tarda who died in an attack of acute porphyria.

Case Report

An unmarried woman born in 1922 was well, with a freckled fair skin, until 1942. There was no relevant family history. In 1942 she noted blistering on her hands only after minor trauma, at any time of the year. In 1945 blisters occurred in warm weather, especially by the sea; if she took her stockings off blisters appeared on her legs; she also had attacks of moderately severe right-sided abdominal pain with constipation. Hospital investigation was inconclusive; appendicectomy showed a fibrosed appendix, but within a week three more attacks of abdominal pain, now with vomiting, occurred; thereafter she continued to blister, though the attacks of pain ceased.

FIG. 1.—Showing crusts on face.

On July 16, 1950, she complained of aching in the legs, pins-and-needles in the hands and feet, swelling of the face, aching breasts, vomiting, frequency of micturition, dysuria, and the passing of dark urine. Her symptoms improved on sulphadimidine, but she was readmitted on July 26. She was plump and cheerful, with a dark, earthy complexion and a slightly swollen face covered with freckles. She had koilonychia of two fingers, no anaemia, and no abnormal physical signs except a blood pressure of 140/90, tenderness in the right iliac fossa, sluggish tendon reflexes, and slight hypotonia. She was very constipated and missed a menstrual period. Investigations were fruitless. On July 22 she complained of an irritating rash on the face and nose.

When seen on August 8 in the routine follow-up she had a yellow skin and conjunctivae, puffy hands and face, with a scabbing eruption of the face (Fig. 1) and a paronychial bullous eruption of the hands. A clinical diagnosis of hydroa aestivale was made, and bilirubin and uroporphyrin were found in the urine; she was again admitted. Three days later more bullae appeared and the oedema diminished, and during the next week the scabs separated, leaving slightly scarred areas. The skin became progressively darker and the sclerae showed pigmentation. Light-sensitivity tests (September 11) on her back showed increased sensitivity to wave-lengths from 1,850 to 3,150 A, maximum at 2,967 A, and two days after the test a fresh crop of bullae appeared on her hands. Some oliguria persisted, and the uroporphyrin and indigoid pigments steadily increased. On October 2, the day after the highest concentration of uroporphyrin was recorded, she developed sudden weakness of her arms, and,

on October 3, symmetrical facial weakness, vocal weakness with a nasal voice, and weakness of neck flexion. There was complete paralysis of the long extensors of the wrist and fingers, and weakness of all other muscles of the upper limbs, the triceps being weaker than the biceps; there was relative spasm of the flexors of the wrist and fingers and of the small muscles of the hand. The lower limbs were weak, and all tendon reflexes of all limbs were absent; plantar responses were flexor. Sensation was normal except for slight impairment to dragged pin below the elbows.

Within six hours all four limbs were completely paralysed and the intercostal muscles were so weak that the patient was placed in a respirator. On October 10 jaundice reappeared; paralysis did not decrease, and on October 14 she died of pneumonia. Permission for necropsy was not obtained.

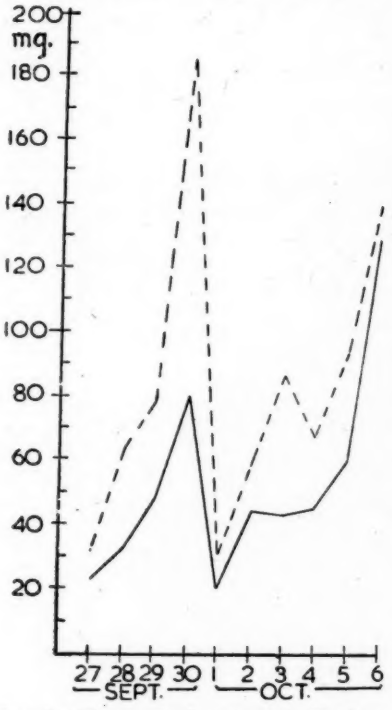

FIG. 2.—Uroporphyrin excretion (Professor Rimington). Continuous line = total excretion, mg. per day. Broken line = concentration, mg. per litre. Note continued oliguria, much less than 1 litre daily.

Results of investigations were all normal except the following: E.S.R. 33 mm. (Westergren) on September 28; serum showed intense red fluorescence in ultraviolet light throughout the last admission; there was slight reduction in serum sodium and chloride from September 5 to October 10, and of potassium to 16 mg. per 100 ml. on October 4 and 6, but this rose to 19 mg. before death; C.S.F. on October 4 had 2 white cells per c.mm., 50 mg. of protein per 100 ml. with excess globulin, Lange 1222321000.

The urinary porphyrin excretion is shown in Fig. 2; a peak was reached two days before the onset of paralysis followed by a fall and a climb to an even higher peak. On admission no porphobilinogen could be detected in her urine, but later the Watson–Schwartz test roughly paralleled the uroporphyrin excretion.

Commentary

Visceral and Skin Changes.—The visceral and cutaneous phenomena of porphyria may be related to an underlying vascular disturbance secondary to the metabolic disorder, as suggested by Waldenström (1937) and Berg (1945). The episodes of colic and hypertension characteristic of the acute disease suggest vascular spasm, and are comparable with the syndrome of lead-poisoning (Discombe, 1948). The skin changes followed the classical pattern of porphyric bullous dermatosis, save that hirsuties was absent. Pigmentation of the conjunctiva is well recognized (Findlay and Barnes, 1950). The paronychial position of the bullae in our case was striking, as was their size, one attaining a diameter of 3 cm.; Dunsky *et al.* (1947) note a miliary paronychial vesicle. Koilonychia persisted in our patient, in spite of normal haemoglobin levels and the administration of iron; Martenstein (1922) and Siemens (1922) note that koilonychia is common in familial hydroa.

Nervous Symptoms.—The paralysis in porphyria may start at any level and may spread either upwards or downwards. Rapid wasting of muscles, with equally rapid recovery, may occur. The paralysis is flaccid, with minimal sensory changes (Boulin *et al.*, 1939; Waldenström, 1939; Barnes, 1945; Symonds, 1949). In the present case slight nervous symptoms were present during the first attack of acute porphyria—fleeting pins-and-needles in the hands and feet without objective sensory changes, and hypotonia and sluggish reflexes without paresis. It is interesting to note that the serum potassium rose after paralysis had become generalized.

Discussion

There can be little doubt that cutaneous porphyria appears when porphyrins are present in the circulating blood. The porphyrin is usually excreted in the urine, but Gray *et al.* (1948), Rimington (1952), van den Bergh and Grotepass (1933, 1937), and Urbach (1937) have described cases in which the urinary porphyrin level was within normal limits, while grossly excessive amounts were excreted in the stools, probably via the bile (van den Bergh and Grotepass, 1937). In such cases it seems that urinary excretion of porphyrin occurs when the patient develops blisters; jaundice often appears at this time.

Porphyrin may be excreted in the urine of subjects who are symptom-free, although so far this has been detected only in the sibs of patients with porphyric bullous dermatosis (Templeton and Lunsford, 1932; Brunsting and Mason, 1946, 1949; Calvy *et al.*, 1951). We are thus led to postulate a syndrome in which porphyrin may be excreted without exciting any symptoms; whereas in some patients who excrete porphyrin the symptoms of a porphyric bullous dermatosis may appear.

The most probable explanation is that low concentrations of porphyrin can be maintained in the blood by an efficient liver, which clears the blood of porphyrin and excretes it in the bile. In such patients no dermatosis occurs, but if the liver is damaged or production of porphyrin is excessive the blood porphyrin rises above the critical level at which dermatosis occurs. Urbach (1936), Szodoray and Sümegi (1944), Brunsting and Mason (1946, 1949), Zeligman and Baum (1948), and Calvy *et al.* (1951) record altogether 32 cases in which chronic alcoholism (with or without syphilis) seems to have been the principal factor in determining the onset of dermatosis; and of Barnes's (1945, 1951) 11 cases, 7 were among Bantus, almost all of whom suffer from a nutritional cirrhosis of the liver. Bolgert *et al.* (1952) record the onset of the disease at age 65 in a sufferer from haemochromatosis.

Templeton and Lunsford (1932) and Orbaneja and Mendoza (1947) have demonstrated a considerable though inconstant increase in urinary porphyrin after solar irradiation, and several of the recorded cases developed symptoms for the first time after excessive exposure to sunlight. The combination of exposure to sunlight and liver damage may account for the high frequency of the disease found in South Africa by Barnes.

Congenital Nature of the Disease.—Porphyric bullous dermatosis is a familial disease. Urbach (1937, Case 1) notes the disease in father and son; Gross (1910) and Hudelo and Montlaur (1919) describe cases in brothers and sisters, while Anderson (1898), Templeton and Lunsford (1932), and Brunsting and Mason (1946, 1949) record cases in which the patient's mother or sister was symptom-free though excreting porphyrin. Borzow (1933) and Calvy *et al.* (1951) describe families with symptoms in sibs of four or five generations.

Hitherto a sharp distinction has been made between congenital porphyria and porphyria cutanea tarda. Search of the reports of the meetings of various dermatological societies found in the *Zentralblatt für Haut- und Geschlechtskrankheiten* suggests that this distinction has little basis in fact (see also Günther, 1922). We have found 147

cases of "congenital porphyria" and "porphyric bullous dermatosis" in which the age of onset is recorded (see Table).

Age at Onset	No. of Cases	Age at Onset	No. of Cases
0–	16	30–	13
1–	8	40–	18
2–	48	50–	8
10–	21	60 +	1
20–	14	Total	147

The case of Schmidt La-Baume (1927) developed symptoms during the second year of life, and was described as "lupus mutilans" when seen after the first decade; that of Marcozzi (1929) passed red urine from birth, but did not develop dermatitis until 2 years old; while the three cases of May *et al.* (1948) all had red urine at birth, grew red teeth, but developed blisters only at the ages of 4, 3, and 1½ years.

We do not think that it is possible to establish reliable criteria by which congenital porphyria can be differentiated from porphyric bullous dermatosis, although the former is usually more mutilating. We suggest that the two are biological variants of a single disease process.

Acute Porphyria and Porphyric Bullous Dermatosis.—The combination of visceral and cutaneous symptoms of porphyria has hitherto been accepted as rare, Gray *et al.* (1948) accepting only 7 cases (Gottron and Ellinger, 1933, 1931; Urbach and Blöch, 1934; Hoerburger and Schulze, 1937; van den Bergh and Grotepass, 1937; Grotepass and Defalque, 1938; Nesbitt and Watkins, 1942; Berg, 1945; Merkelbach, 1943; Taylor *et al.*, 1946; Linas *et al.*, 1947). We have found at least 22 more cases recorded in the literature (Thiele, 1924; Berckel, 1926 (2 cases); Loewenstein, 1937; Borda, 1945 (3 cases); Kuske, 1946; Brunsting and Mason, 1949 (case 1); Calvy *et al.*, 1951 (4 cases observed, presumptive evidence of 3 more); Barnes, 1945, 1951 (at least 6 cases). These reports show that the dermatosis may either precede or follow the abdominal symptoms.

Conclusion

We suggest that the classification of the porphyrias could be simplified as follows:

1. Visceral porphyria, equivalent to Waldenström's acute porphyria and Watson's intermittent acute porphyria.

2. Cutaneous porphyria, a condition essentially congenital, but becoming manifest at any time from birth to death. Manifestation appears to depend on increase in blood porphyrin, and may be determined by biological or congenital factors, by some acquired factor such as hepatic dysfunction, or by some external factor such as excessive solar irradiation.

3. Mixed porphyria, in which symptoms of one form appear in a subject affected by the other.

Taking the scheme of Rimington (1952) as a basis, the cutaneous porphyrias would have deficiencies in the enzymes needed for the further metabolism of porphyrins *sensu stricto*, while the visceral porphyrias would have a defect in the enzyme system responsible for the building up of pyrrole units into porphyrins. Both enzyme systems might be affected by environmental factors, and might well share some essential component.

Summary

A case of porphyria cutanea tarda in which the patient developed constipation and abdominal pain and died with widespread paralysis is described.

It is suggested that no reliable criteria exist by which "congenital porphyria" can be differentiated from "porphyria cutanea tarda," and that the two are biological variants of a single disease process.

The classification of the porphyrias is reviewed, and it is suggested that the most satisfactory classification is into visceral, cutaneous, and mixed forms.

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PARTIAL HEPATECTOMY

OBSERVATIONS ON AN ILLUSTRATIVE CASE

BY

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The accepted indications for partial hepatectomy are not many. Apart from the local removal of portions of liver tissue for examination under the microscope, or to allow exposure of the main ducts in the neighbourhood of the hilum for the purpose of repairing injuries, the main indications for planned resection of portions of the liver are the removal of hydatid cysts and of innocent tumours, usually hepatic adenomata or angiomata. Partial hepatectomy for malignant disease can very rarely be justified. Primary cancer arises either in the gall-bladder and is not discovered until it has invaded the portal fissure and caused jaundice, or in the liver cells when it takes the form of a diffuse malignant infiltration of the whole organ. Secondary metastases are nearly always multiple, and it can be assumed that many further seeds of cancer, still impalpable, are scattered throughout the liver.

In the case here reported the patient, a very fit young man of 30 who was about to be married, had a single large metastasis occupying the dome of his liver and

bulging up the diaphragm a short distance in front of the opening for the inferior vena cava. The primary tumour in the rectum had been removed. The secondary deposit in the liver had been known to be there for about two years, and had not increased greatly in size. Removal of this tumour with an adequate margin of surrounding liver tissue would in all probability remove the only malignant cells remaining in his body. The chance of turning the signals from red to green at the age of 30 seemed worth a considerable risk.

Case History

A man, 28 at the time, was operated on in 1949 at a hospital overseas for a small tumour the size of a cherry situated in the posterior wall of his rectum about three inches (7.5 cm.) above the ano-rectal ring. The surgeon took a piece of the tumour for section, which was reported as a carcinoma. He then did a laparotomy, at which he found a number of enlarged glands in the mesorectum, some nodules in the pancreas, and a single lump on the diaphragmatic surface of the right lobe of the liver. He removed a gland the size of a pigeon's egg from the hollow of the sacrum, and took a piece of the tumour in the liver for section. Both of these specimens were reported by the pathologist to contain deposits of the same nature as the tumour in the rectum. The surgeon gave the relatives, but not the patient, a hopeless prognosis.

A year later, in the summer of 1950, the young man came to Britain with his family to attend the Edinburgh Festival. He was still apparently well, but was persuaded to consult me by his brother, who meanwhile had given me the whole story. He walked into my consulting-room, one of the fittest athletes I have seen, tall, lean, muscular, bronzed, and bursting with vitality. He had had no symptoms, he had lost no weight. He had one discoverable abnormality only—a tumour the size of a cherry in the back wall of the rectum, of rubbery consistency and slightly fixed to the sacrum. I told the brother that I had been unable to find anything to justify a gloomy prognosis, but that I could not give a firm opinion until I had seen the sections.

A month later I received the sections and the blocks from which they had been made. Dr. de Navasquez reported that one showed an argentaffin tumour of the rectum, the second a lymph node infiltrated with argentaffin cells. As most London surgeons do when in difficulty, I consulted Dr. Cuthbert Dukes. He agreed with the diagnosis, and explained that, while most argentaffin tumours are innocent and remain local, some metastasize, but the metastases are usually few and scattered, and, like the primary tumour, grow very slowly. In view of Dr. Dukes's opinion, I advised the patient and his parents that an attempt should be made to remove the primary tumour and its extensions. He arranged to come to England the following year.

The removal involved four stages.

First Operation (May, 1951).—Laparotomy. A number of glands varying in size from a walnut to a pea could be felt in the mesorectum, and one was adherent to the left lateral wall of the pelvis near the ureter, but there were no palpable glands above the pelvic brim. The pancreas felt normal. A round lump the size of a billiard ball could be felt projecting upwards from the dome of the right lobe of the liver, but could not be brought into view. A transverse colostomy was done.

Second Operation (June, 1951).—The rectum with the lower half of the pelvic colon, the pelvic mesocolon, and all the tissue in the hollow of the sacrum were removed down to a level one inch (2.5 cm.) below the rectal tumour and two inches (5 cm.) above the ano-rectal ring. The enlarged glands were dissected off the left ureter with scissors. The pelvic colon was anastomosed end to end to the stump of the rectum under some tension, and the suture line later gave way in part.

Third Operation (August, 1951).—The metastasis in the liver was removed by the transthoracic transdiaphragmatic approach.

In all three operations I was helped by my colleague Mr. Guy Blackburn.

Fourth Operation.—Closure of colostomy performed in his home country in January, 1952. The parting of the anastomosis had left him with a pelvic fistula that took six months to heal, and, until it had healed, the colostomy had to remain open.

Discussion

The only part of these operations that is relevant to the present communication is the removal of the hepatic metastasis. The laparotomy had made two things clear—that this tumour could not be brought into view or reached with instruments by a purely abdominal approach, and that it burrowed deeply into the liver substance, and must extend pretty close to the visceral surface and to the main branches of the portal vein and the bile ducts. An abdomino-thoracic approach had no advantages in this case over a purely thoracic one: after a fair trial I hold to-day that this approach is wrong, anyway. The wide combined incision cuts a lot of muscles that need not be cut; it divides unnecessarily a lot of vessels that must be clamped and ligated; it submits the patient to the physiological difficulties of an open thorax for a far longer time than is necessary; and it adds to those difficulties by casting off the moorings of the diaphragm and, indirectly, of the pericardium. Any operation that can be done through an abdomino-thoracic incision can be done better through an abdominal incision, which is closed when 90% of the job has been done, and finished off through a thoracotomy.

The thorax was opened by an incision through the whole length of the eighth rib bed, a rib spreader was inserted, and the lung was packed out of the way. The diaphragm was incised radially over the tumour for a length of seven or eight inches (17.5–20 cm.), allowing the liver to bulge through it. The tumour, covered by a layer of normal liver projected from its surface like a large blister. The diaphragmatic edges were retracted, allowing the liver to prolapse further, and acriflavine gauze was packed all round to prevent blood trickling down into the abdomen.

The question was—how much blood? Previous experience of the instructions of textbooks had left me unconvinced. A wedge biopsy of a cirrhotic liver is a straightforward affair; haemorrhage is moderate and suture of the gap is easy. A wedge removal of normal liver tissue varies from messy to alarming. The method of interlocking sutures of catgut passed through the liver with blunt needles parallel to the line of the proposed incision and tied before it is made—a method usually illustrated by the convincing drawings of a professional artist—just does not work. Normal liver has the consistency of cheese, and sutures cut through it long before they have been drawn tight enough to arrest haemorrhage. Fortunately the bleeding, alarming at first, stops when the sides of the wedge are brought together. It was quite clear that any wedge adequate to include this tumour would bisect the liver. I asked Guy, "What do we do now?" He replied, "I don't know what we do now, but in five minutes we shall be rushing him back to bed with a pint of blood running into each arm as fast as we can push it."

The first incision into liver outside the edge of the swelling produced an alarming gush of blood, which was soon seen to be coming from a divided vessel. In securing this vessel it was clear that the haemostat cut through liver tissue like butter, but met with a resistance that could be appreciated when it reached the firmer tissue of Glisson's capsule in which the bleeding vessel lay. Thereupon the knife was laid aside. A fine-pointed haemostat was used, closed, for cutting the liver substance by very slow and gentle strokes made parallel to and about a centimetre outside the margins of the tumour. The instrument cut through liver parenchyma almost bloodlessly. It gave a sense of slight resistance when-

ever it met a fibrous septum. It was thereupon clamped on the band, which was ligated and cut. The dissection went on slowly round the tumour, which was lifted up as it became free. Some of the bands encountered were tiny, some were of moderate size, but none were really large. When the tumour was finally removed the cavity left in the liver was like a tea-cup, oozing slightly from its whole surface, but not bleeding from any particular point. The total blood loss cannot have been more than three or four ounces (85–115 ml.).

It was clear that such a cavity could not be closed. A long forceps was therefore passed down between the diaphragm and the liver till its point could be seen bulging the abdominal wall at the costal margin. An incision was made over the point and a strip of corrugated rubber was drawn back and laid in the cavity. The diaphragm was repaired, the lung re-expanded, and the thoracotomy incision closed.

Dr. de Navasquez reported as follows on the specimen: "The specimen shows a spherical tumour 8 cm. in diameter which is an argentaffin tumour or 'carcinoid' of similar morphology to the tumour in the rectum. The excision appears to be complete, as the tumour is surrounded by normal liver."

The patient was slightly jaundiced for a few days after the operation, but his condition was never alarming. Drainage was maintained for about a week. He is now back at his work as a fruit farmer, playing games, and feeling well. He has gained 30 lb. (13.6 kg.) in weight. He has lost his fiancée, who was more upset by the series of operations than he was, and threw him over. Perhaps he has gained more by his ordeal than he realizes.

Conclusion

I cannot claim to be familiar with the literature of partial hepatectomy, nor have I consulted more than the standard textbooks of operative surgery. It would, in any case, be out of place to burden a clinical report of a single case with references to the experience of others.

The surgeon to-day is confronted with the almost impossible task of keeping in touch with a literature that increases in volume every year. He can read most of that which concerns the small branch in which he is particularly interested. For the rest he must be content to let others do the hard work at the coal face, and get the knowledge from them, picked, assorted, graded, and delivered in clean sacks. The knowledge thus acquired gains in perspective from being unclogged by excessive detail, and it is laid down in the association centres of a mind clarified by idleness. What I have learned of surgery since taking my Fellowship has been gleaned from registrars, house-surgeons, dressers, and sisters; from meetings of the Association of Surgeons, the Royal Society of Medicine, and the Medical Society of London; from journeyings round Europe with the Surgical Travellers; and from the Colchester Surgical Group and those who visit them. At a recent Colchester meeting we were discussing the surgery of the liver, and I learned for the first time that the method that proved so useful to me in this case was not known to the majority. For that reason, because the information may prove useful to others faced with a similar predicament, I venture to put out this unscientific communication.

The use of radioactive phosphorus to study the movements of wild rodents over a long period has had promising results. Workers at the University of Wisconsin have found it possible, with the help of a Geiger counter, to trace the movements of a field-mouse, which had previously been injected with a harmless amount of radioactive phosphorus, by its radioactive excretions. These tests have shown that a field-mouse travelled at least 700 feet in a period of eight days, and ranged over an area of 120 feet long and 100 feet across. The method has also been used in tracing the movement of insects and birds.

PLASMA PROTEIN CONCENTRATION OF NORMAL ADULTS LIVING IN SINGAPORE

BY

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Wills and Bell (1951) and Holmes *et al.* (1951) found that coloured people living in the Tropics had higher plasma protein concentrations than white people living in the same climate. The present investigation was designed to show whether a racial difference in plasma protein concentration did exist under good social conditions and to show whether the plasma protein concentration of healthy people was the same in the Tropics as in a temperate climate.

Materials and Methods

The subjects were students, blood-donor volunteers, or members of the armed Forces, between 20 and 40 years old. All were apparently in good health, and in a state of adequate nutrition. There were 80 men, of whom 24 (30%) were Asian (Chinese, Eurasian, or Indian) and 56 (70%) European. There were 59 women, of whom 17 (29%) were Asian and 42 (71%) European.

Venous blood samples were collected with minimal stasis, and the oxalate mixture of Heller and Paul (1934) was used as an anticoagulant. The subjects were recumbent for a few minutes before and during the collection of the blood. The samples were kept in stoppered bottles and stored at about 4° C. until required. Estimations were made within a few hours of collection, except in a few instances in which there was a delay of 24 hours. Plasma was obtained by centrifuging the blood in stoppered tubes. Before transferring the blood to these tubes it was thoroughly mixed in the storage bottles.

Estimations of the specific gravity of the plasma were made by the method of Phillips *et al.* (1950) and the results converted to equivalent total protein concentration by the application of a suitable formula. It was necessary to determine which of the formulae suggested by previous investigators (Moore and Van Slyke, 1930; Kagan, 1938; Phillips *et al.*, 1945; etc.) was the most suitable in the present instance. Simultaneous estimations of the specific gravity and of the total nitrogen content were therefore made on 25 samples of plasma obtained from men and women. These were sometimes pooled if individual quantities were insufficient for analysis. The total nitrogen was estimated by the macro-Kjeldahl method and converted to the equivalent amount of total protein by multiplying by 6.25 (Hawk *et al.*, 1947). Duplicate and blank determinations were made in each instance. In making these estimations 1 ml. of plasma was treated with 20 ml. of concentrated sulphuric acid. A mixture of copper sulphate (0.1 to 0.2 g.) and potassium sulphate (5 to 10 g.) was added. Digestion was continued for four to five hours after the mixture became clear.

In a separate investigation it was found that the same results were obtained on prolonging the oxidation for 10 hours. The method was found accurate when applied to a standard solution of ammonium sulphate of known nitrogen content. Recovery experiments were also made, using preserved ox plasma to which known amounts of nitrogen from a standard ammonium sulphate solution were added. There was always a recovery of at least 87%.

Results

The most suitable formula for converting specific gravity measurements to total protein concentration in the present investigation was that proposed by Phillips *et al.* (1945), if no correction was made for the presence of oxalate. This formula was :

$$P = 360\ (s - 1.007)$$

where P was the total protein in grammes per 100 ml. and s was the observed specific gravity of the plasma specimen. The mean plasma protein concentration of the 25 samples estimated from total nitrogen content was 7.68 g. per 100 ml., and that derived from specific gravity measurements was 7.67 g. per 100 ml.

Applying the above formula to specific gravity measurements, the mean plasma protein concentration of 80 men was 7.8 g. per 100 ml., and of 59 women 7.6 g. per 100 ml. The difference between the mean plasma protein concentration of Asians and that of Europeans was not statistically significant either for men or for women. The difference between the mean figure for men and that for women was also not significant. Details are given in the Table.

Plasma Protein Concentration of Healthy Men and Women Living in Singapore

Group	No.	Plasma Protein (g./100 ml.)	S.D.	S.E. of Mean	"t"	P
Males						
Asian ..	24	7·69	1·682	0·3433	0·62	50
European ..	56	7·89	1·136	0·1517		
Females						
Asian ..	17	7·78	2·025	0·4911	0·58	50
European ..	42	7·53	1·246	0·1922		
Combined Groups						
All males ..	80	7·84	0·987	0·1103	1·4	10
,, females	59	7·59	1·106	0·1439		
,, samples	164	7·7	1·31	0·1023		

The grand mean of all estimations made by the specific gravity method for plasma protein concentration of 80 men, of 59 women, and of 25 samples used in the course of the comparison with total nitrogen estimations was 7.7 g. per 100 ml.

Discussion

Marrack and Hoch (1949), on reviewing the available literature, concluded that the mean total protein concentration of normal adults approximated to that found by Gutman *et al.* (1941)—namely, 7.2 g. per 100 ml. These estimations, however, were made on serum and not plasma. Even so the present findings suggest that living in a warm climate may be associated with a relatively high plasma protein concentration which is not caused by dehydration or increased formation of antibodies. An investigation of haemoglobin levels (Wadsworth, 1953) and of packed red cell volume (Wadsworth, 1952) did not suggest that healthy people living in Singapore suffered from haemoconcentration due to excessive loss of moisture from the body. Wills and Bell (1951) suggested that the comparatively high plasma protein concentration of the coloured subjects of their investigation might have been due to a high antibody content of the blood; but Singapore is free from chronic endemic infections which might give rise to such antibody formation, and no increase of the plasma protein concentration can be expected from such a cause.

Although an ammonium salt was used in the present investigation in the anticoagulant mixture, the amount was too small to affect the results of the total nitrogen estimations.

The experiments of Bazett (1949) suggested that the amount of protein in the plasma varied in such a way as to counteract the movement of fluid from the blood into the tissue spaces. A high concentration of plasma proteins in the blood of people living in the Tropics may therefore be the result of a compensatory change to prevent an excessive loss of fluid from the blood into the tissue spaces.

It is necessary to state that the present investigation was not concerned with the universal application of a particular formula for the conversion of plasma specific gravity to total protein concentration. The formula adopted was found accurate when applied to specific gravity measurements made in the circumstances of the present investigation, but it does not follow that it would yield accurate results when applied to such measurements made elsewhere. The discrepancy between results of investigations of total plasma protein concentration made by different authors indicates that more rigid standardization of technique should be used if the influence of climate and other factors on this value is to be accurately assessed. In the absence of such standardization each series of determinations must be checked against some method of known accuracy.

Summary

The plasma protein concentration of 80 men and 59 women was measured by the copper sulphate specific gravity method, and found to be 7.8 g. and 7.6 g. per 100 ml. respectively.

The accuracy of the method was tested against estimations of total nitrogen made by the macro-Kjeldahl method. Close agreement was found between the two series of estimations.

The difference between the mean plasma protein concentration of Asians and that of Europeans was not statistically significant.

The findings suggest that living in a warm climate might be associated with a relatively high plasma protein concentration which is not a result of dehydration or of increased antibody formation.

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Last financial year (1952–3) the British Council's grant from United Kingdom public funds was cut by 8% to just over £2.5 million. In the annual report giving these figures, the council devotes a chapter to its work in science and medicine. The British Council makes no attempt to interpret science to the general public overseas, but addresses itself solely to professional associations and universities. It does this by providing facilities for personal contacts between scientists, by distributing and publicizing scientific material, and through its own publications. In the medical field last year the council sponsored 12 overseas lecture tours or advisory visits by eminent British medical workers; it helped arrange the programme of nearly 500 foreign students, research workers, and medical visitors; it arranged for the showing of British medical films abroad; and it published the *British Medical Book List*—a guide to new medical publications for overseas booksellers—and the *British Medical Bulletin*. In addition the council has carried out a survey of medical, scientific, and engineering graduates who either visited or left Britain for the purpose of advanced study and research. Of these 40% were medical.

FAILURE OF ANTIBIOTICS IN A CASE OF STAPHYLOCOCCAL BACTERIAEMIA

BY

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Penicillin-resistant staphylococci are now so frequently encountered in hospital practice that reliance often has to be placed on the newer antibiotics in treating infections due to these organisms. The following case history is of particular interest in that aureomycin and chloramphenicol failed to cure penicillin-resistant staphylococcal bacteriaemia in spite of (1) being effective against the organisms *in vitro*, and (2) the absence of a demonstrable focus of infection. Nichols and Needham (1949) mention a somewhat similar case, but with a much shorter illness.

Case Record

A West African nurse aged 26 was admitted to North Middlesex Hospital, under the care of Dr. Norman Whittaker, with a fever (102° F.—38.9° C.) and a four-days history of pains in the back of the neck following upon the healing of a small furuncle in the nose. She gave a past history of malaria and of appendicectomy.

No abnormal physical signs were discovered. The urine and C.S.F. were normal, blood films revealed no malaria parasites, and leucocytes totalled 8,900 per c.mm., with 80% polymorphs. The fever persisted despite penicillin, and two blood cultures grew *Staphylococcus aureus* sensitive to aureomycin and chloramphenicol, relatively resistant to streptomycin, and resistant to penicillin. A 10-days course of aureomycin (0.5 g. six-hourly) was given in place of penicillin. Fever subsided in 48 hours, but recurred two days after the end of the course and blood culture again grew *Staph. aureus*. This story was repeated after a second and a third course of aureomycin lasting 31 days and 48 days respectively. On her fourth course of treatment, lasting 34 days, *Staph. aureus* was grown from the blood while she was afebrile and still taking aureomycin. Fever recurred during the latter part of this course, with yet another positive blood culture, and the patient was transferred to the care of Sir Neil Hamilton Fairley at the Hospital for Tropical Diseases.

During her stay in the North Middlesex Hospital all attempts to find a focus of infection failed, and white-cell counts varied between 6,200 and 9,600 per c.mm. Full radiological investigations of the teeth, sinuses, chest, and skeleton proved negative. Intravenous and retrograde pyelography showed the kidneys to be horse-shoe in type and functioning normally.

On admission to the Hospital for Tropical Diseases a blood culture yielded a heavy growth of coagulase-positive *Staph. aureus* sensitive to aureomycin and chloramphenicol, and a fifth course of aureomycin was given for 14 days. Temperatures became normal after nine days but rose again the day after stopping treatment, and blood culture now grew *Staph. aureus* sensitive only to chloramphenicol while moderately sensitive to aureomycin, streptomycin, and oxytetracycline (terramycin). The organism was sensitive to 5 μg. of chloramphenicol per ml. A course of this antibiotic was given until the patient died 57 days later, the dosage being 0.5 g. six-hourly for the first week and 1 to 1.5 g. six-hourly thereafter. On the lower dosage a blood level of 20 μg. per ml. was obtained in a sample of venous blood collected six hours after a dose. In spite of this the organism was repeatedly recovered on blood cultures, even with the high dosage. Complete E.N.T. and gynaecological examinations revealed no septic focus, and urinary deposit was consistently normal. The leucocyte count remained below 10,000 per c.mm., with about 75% polymorphs, until the final stage, when it rose to 13,200. The haemoglobin dropped steadily, and repeated blood transfusions were given with little avail. Bronchopneumonia closed the scene after an illness lasting 226 days.

A detailed post-portem examination was carried out by Dr. D. S. Ridley. The lungs were oedematous and there was a patch of bronchopneumonia at the left base. The heart and its valves and arteries were normal. The spleen was rather enlarged but not soft or septic. The kidneys were horse-shoe but otherwise normal. No evidence of sepsis or other abnormality was found in the liver, intestines, gall-bladder, pancreas, suprarenals, ovaries, uterus, bladder, brain, mastoids, maxillary and frontal sinuses, and spine. No enlarged glands and no infarcts were found. Histological examination revealed nothing further.

Discussion

It may be argued that antibiotics failed owing to a localized infection somewhere in the body. No such focus was found in spite of comprehensive clinical, laboratory, radiological, and post-mortem examinations.

The development of staphylococcal resistance to aureomycin and chloramphenicol may be postulated. It was not until the fifth month of her illness, however, that some resistance to aureomycin occurred, after a total dosage of 178 g. Treatment was then changed to chloramphenicol, and no resistance of this particular strain to chloramphenicol was found on repeated *in vitro* tests.

The dosage of antibiotics may be considered. Aureomycin was given in five courses of 1 to 2.5 g. daily over a total period of 137 days. With chloramphenicol the blood level was estimated. The Oxford staphylococcus used as a standard is sensitive to 5 μg. of chloramphenicol per ml. This staphylococcus was equally sensitive. A blood level four times the *in vitro* level is recommended in treatment (Pharmaceutical Society, 1952) and was achieved here on a dosage of 0.5 g. six-hourly, but pyrexia and positive blood cultures persisted even when the dosage was raised.

Aureomycin and chloramphenicol act on bacteria by inhibiting growth rather than by direct bactericidal action, and radical cure of an infection is ultimately dependent on the defensive mechanism of the body itself. This patient may have had a defective cellulo-humoral response, for throughout her illness the total neutrophils were lower than would normally be expected in staphylococcal bacteriaemia.

Summary

A young African woman developed staphylococcal bacteriaemia following a small furuncle in the nose, the organism being sensitive only to aureomycin and chloramphenicol. In spite of five courses of the former (total 178 g.) and one course of the latter (252 g.) the organism persisted in the blood without any focus of infection being found. A blood concentration of at least 20 μg. of chloramphenicol per ml. failed, although *in vitro* tests showed the staphylococcus to be sensitive to 5 μg. per ml.

We are grateful to Sir Neil Hamilton Fairley for his advice, to Dr. Norman Whittaker for permission to publish this case, and to Dr. D. S. Ridley for his post-mortem report.

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MALARIA IN NEIGHBOURING LONDONERS

BY

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Although cases of primary malaria in England have been recorded from time to time (*British Medical Journal*, 1950), including several arising in London (Fermont, 1947; Blaxland Levick and MacGregor, 1947), the occurrence of malaria in neighbours, within a few weeks of one another, seemed unusual enough to warrant an account.

Case 1

A housewife aged 27 was admitted to Lambeth Hospital, under the care of Dr. A. A. Guild, on August 7, 1953, complaining of fever and headache. She noticed that her fever came on alternate days.

In May, 1953, she had had a febrile illness at home which was thought to be pneumonia, but chest radiographs taken at that time showed no definite abnormality. The illness had lasted five weeks, and the temperature then had not shown the periodicity which was a feature of her present illness. In August, 1952, the patient had visited Nice, and, with her husband, made trips into the surrounding country.

On examination the spleen was enlarged 3 in. (7.5 cm.) below the costal margin and her temperature rose on alternate days to 104.2° F. (40.1° C.). The blood films showed fairly numerous parasites of *P. vivax*, including gametocytes. She was treated with mepacrine, 200 mg. eight-hourly for 48 hours and then 100 mg. eight-hourly for 24 hours, followed by primaquine, 10 mg. daily for 14 days.

As her peripheral blood contained gametocytes and her fever was of the classical tertian type it was thought that this was not her first attack and that her illness the previous May was probably the primary attack.

Case 2

A boy aged 8 years was admitted to the Royal Waterloo Hospital under the care of Dr. B. D. R. Wilson on June 30, 1953. He had been referred for the investigation of attacks of shivering with splenomegaly. Until one month before admission he had been perfectly well. He then began to have recurrent feverish attacks. These started suddenly with malaise, followed by a feeling of coldness and shivering. After about three hours he started sweating and became flushed. In another three hours the episode was over. The attacks occurred on alternate days, and in between each attack he felt quite well. There was no history of any febrile illness in the preceding two years. The patient had lived in London since the age of 2, and his most recent trip was to the Isle of Sheppey in 1951.

He had an irregularly remittent pyrexia during his first four days in hospital, ranging from 99° to 101° F. (37.2 to 38.3° C.). His spleen was enlarged about 2 in. (5 cm.) below the costal margin. Parasites of benign tertian malaria were found in the blood.

The boy was treated with chloroquine, 0.45 g. stat., 0.3 g. twice daily for three days, followed by pamaquin, 5 mg. three times a day for 12 days. His fever did not recur after the start of the treatment, and his spleen diminished in size until only the tip was palpable, when he was discharged (August 8).

This was thought to be a primary malarial attack.

Discussion

These two patients live in adjacent semi-detached houses in Stockwell (South London). Each house has a small garden containing several poorly lit sheds and patches of thick undergrowth. In one garden there was a large pigeon loft and an enclosure containing a dog, while in the other there was a discarded tank half full of stagnant water. No mosquitoes or larvae were found in the houses or gardens when we visited them in August, 1953, but on waste ground near by numerous mosquitoes were captured among some sprouting tree-stumps. These, disappointingly, proved to be culicines.

The possible modes of infection in these two cases were: (1) The first patient contracted malaria during her visit to Nice, and this was transmitted during May to the boy. Against this may be set the fact that malaria is not endemic in the Nice area (P. G. Shute, personal communication). (2) Both cases contracted malaria in Stockwell from a third person recently returned from a malarious area. No such person was known to be living in the vicinity. This, of course, does not rule out the possibility. (3) Each case acquired malaria independently elsewhere. Neither case had ever received a blood transfusion or injection. Inquiries into the possibility of malarious mosquitoes, used for therapeutic purposes, having been released in the neighbourhood produced negative results. The boy had not been out of London for two years.

Since the third possibility seems too much of a coincidence, it must be assumed that transmission was via local anopheline mosquitoes.

The following three species may be found in London: *A. maculipennis*, the most widespread anopheline in this country, will breed only in natural collections of water, of which there are none locally. Moreover, the variety atroparvus, the one most likely to transmit malaria in Britain, breeds in coastal salt waters (Marshall, 1938a). *A. claviger*, however, will breed in tanks (Marshall, 1938b). *A. plumbeus*, a tree-breeding type, has been shown experimentally to carry malaria, and is common in London (H. I. Leeson, personal communication).

Either *A. claviger* or *A. plumbeus* was the likely vector in these cases, and the fact that they were not caught locally in August does not rule out their presence there during the previous May.

We should like to acknowledge the help received from Major H. I. Leeson, of the London School of Hygiene and Tropical Medicine, and from Mr. P. G. Shute, of the Malaria Reference Laboratory, Horton. We are grateful to Dr. B. D. R. Wilson and Dr. A. A. Guild for permission to record these cases.

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Professor Frederick Heaf, David Davies Professor of Tuberculosis at the University of Wales, left London by air on November 15 for Turkey, where he is to lecture, under British Council auspices, on tuberculosis and discuss preventive measures with Turkish specialists in Ankara and Istanbul. His visit is at the request of the Turkish Ministry of Health, and he will be there for three weeks. He is then to visit Greece from December 6 to 12, and will lecture to medical societies in Athens and Salonika. In Istanbul he will lecture to a congress of doctors, arranged by the World Health Organization, which begins in the first week of December. Medical men from 16 countries will attend, and the Congress includes special courses on tuberculosis. Professor Heaf's lectures will include the prevention, diagnosis, and treatment of tuberculosis, and anti-tuberculosis vaccination. In Turkey and Greece, British films on tuberculosis will be shown in connexion with the lectures.

Medical Memorandum

Granulocytopenia Occurring During Sodium Gentisate Therapy

Sodium gentisate, an oxidation product of salicylic acid, was introduced to clinical medicine by Meyer and Ragan (1948), who found that, like salicylates, it inhibited the spreading power of hyaluronidase. They used it in a small series of cases of acute rheumatism and found that it had an antirheumatic effect. Camelin *et al.* (1949, 1950), who studied its clinical use in more detail, believe it to be as effective as sodium salicylate without the latter's toxic side-effects. They gave sodium gentisate in doses of up to 20 g. a day by mouth without noting any constitutional reaction or change in the blood picture.

Both the following cases were given 10 g. of sodium gentisate daily by mouth during the treatment of attacks of acute rheumatism, and both developed neutrophil leucopenia with an absolute lymphocytosis. In one case these blood changes were detected during the administration of the drug, in the other during the weeks following its withdrawal.

CASE 1

A girl aged 13 developed a sore throat three weeks before admission to hospital. Two weeks later she became feverish and complained of headache, backache, and pain and swelling of the right knee and the right first metatarso-phalangeal joint.

On admission five days later she was ill and febrile and the knee-joint was still swollen and tender, though physically she was otherwise normal. Salicylates were not started at once, but within 48 hours the arthritis had shifted to involve the left knee-joint and both ankle-joints. At this stage she was given sodium salicylate, 120 gr. (8 g.) daily, with an equal quantity of sodium bicarbonate. Her temperature dropped during the next two days and the pain in her joints disappeared. On the eighth day after admission her E.S.R. was 40 mm. in one hour (Wintrobe), and her white blood cells numbered 7,650 (neutrophil polymorphs 30%, lymphocytes 61%, eosinophils 7%, monocytes 2%). Her haemoglobin was 70%.

The salicylate course was continued for another 18 days, but, as she was having a slight evening fever, her appetite was poor, and she was complaining of some tinnitus, it was decided to stop the salicylate and to change to sodium gentisate, 10 g. daily. This treatment was continued for three weeks, the dose being then reduced to 5 g. daily. One month after the start of gentisate therapy a further blood count showed a total of 11,650 cells, with 5% polymorphs and 95% lymphocytes. Her haemoglobin was 92%. One week later her polymorph count was unaltered, so it was decided to abandon the sodium gentisate, which it was thought might be a leucotoxic agent. The possibility that the blood changes might be due to a virus infection was considered, but there was nothing on clinical examination to support this view. Her Paul–Bunnell reaction was negative to a dilution of 1/640.

Serial blood counts showed a polymorph leucopenia persisting for a further three weeks and then only gradually returning to normal figures. Her lymphocyte count remained somewhat high. Clinically she had completely recovered by the end of the second month and her E.S.R. was down to normal limits, yet at this time her polymorphs numbered only 630 cells per c.mm. A sternal puncture was later performed, though not until the eighteenth week, when the blood picture was starting to recover. The marrow was richly cellular and entirely normal. A chest *x*-ray film at this time had shown a normal heart and lungs, and shortly afterwards she was discharged to convalescence. Three months later her total white count was 6,200 cells, with 55% neutrophil polymorphs and 32% lymphocytes.

CASE 2

A girl aged 14 developed a swinging fever with pain and swelling of both wrist-joints and elbow-joints 10 days before admission to hospital. She had been treated with sodium salicylate by her own practitioner. The joint pain and swelling had subsided in a couple of days and her fever had lessened, but she had remained ill and toxic and was sent to hospital.

On admission she had a low fever, her joints were normal, and her heart was not enlarged, though a harsh systolic murmur was heard at the pulmonary area. Her E.S.R. was 24 mm. in one hour (Wintrobe), and an electrocardiogram showed a corrected Q–T interval (Q–Tc) of 0.423 second. Her rheumatism still seemed to be active, so she was put on to 10 g. of sodium gentisate daily by mouth. No white blood cell count was done until one week later, when it was 8,400 (47% polymorphs, 52% lymphocytes). Her E.S.R. had fallen to 8 mm. in one hour and she was clinically improved. Sodium gentisate was stopped after four and a half weeks, when her white-cell count was within normal limits. The count then started to drop, the polymorphs reaching a minimal figure of 750 per c.mm. five weeks after stopping treatment but thereafter tending to recover. She never became anaemic, and at no time was there any clinical indication that she might have suffered any superadded infection capable of affecting her blood count. A chest *x*-ray film taken late in her stay in hospital showed no abnormality, and after 17 weeks under observation she was discharged to convalescence. Three months later her total white-cell count was 8,750 (55% polymorphs, 37% lymphocytes).

COMMENT

Fairly full descriptions of these two cases have been given to show that both were typical of rheumatic fever. No other drug was given to either case during or after the course of sodium gentisate, so that this cause of granulocytopenia can be dismissed. The maintenance of normal haemoglobin levels throughout the time when the polymorph count was depressed excludes the possibility of a generalized effect on haemopoiesis from the acute rheumatism itself. Acute rheumatism in its active stages is a well-known cause of polymorph leucocytosis (Hubbard and McKee, 1939), and I can find no record of a leucopenia being attributed to it at any stage in the disease. It must, however, be noted that in Case 1 there was some depression of the polymorph count in the early stages, when salicylates were still being given. Nevertheless it seems probable that the granulocytopenia with its associated lymphocytosis was due to the effect of sodium gentisate. This may have resulted from an idiosyncrasy to the drug reminiscent of the effect of amidopyrine. Camelin *et al.* did not find any alteration in the blood picture in their series of cases treated with sodium gentisate, while Schaefer *et al.* (1950), who gave their cases 18 g. of sodium gentisate daily, found a polymorph leucocytosis in two patients who developed septic complications while on this treatment. It therefore seems unlikely that granulocytopenia will prove to be a common complication of gentisate therapy, but whenever the drug is used it would be advisable to keep a watch on the total and differential white counts both during and for a few weeks after its administration.

I am indebted to Dr. M. S. Ross, of the Group Pathological Laboratory, Queen Mary's Hospital for the East End, London, E.13, for the blood examinations and for the sternal biopsy.

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Reviews

CONQUEST OF PLAGUE

The Conquest of Plague: A Study of the Evolution of Epidemiology. By L. Fabian Hirst, M.D., with a foreword by Lieutenant-General Sir William MacArthur, K.C.B., M.D., F.R.C.P. (Pp. 478; illustrated. 42s.) Oxford: Clarendon Press. 1953.

In these days, which have seen the conquest of so many epidemic diseases, the people of Great Britain hardly realize what a perpetual menace these diseases were to their ancestors. Those who remember the pandemic of influenza in 1918–19 may recall something of this universal apprehension. In mediaeval times "the pestilence that walketh in the darkness" was as much to be feared as "the arrow which flieth by day," while the high mortality, the despair, and the terrible incidents of the Great Plague of 1665 are vividly described in Defoe's *Journal of the Plague Year.*

The word "plague," derived from the Latin *plaga,* means a stroke. According to Professor Singer* the word first appears in Wycliffe's translation of the Bible in 1382. There are many descriptions of early epidemics of plague in literature, as in the Bible, where the plague of Ashdod (I Samuel v. and vi.) was characterized by "emerods," the inguinal swellings or buboes of plague. Procopius gave an accurate record of the great outbreak at Constantinople in A.D. 542, when Justinian was emperor. It arose in Egypt and followed the trade routes; beginning at the ports, it spread inland. Procopius also observed that those who had recovered were immune from infection and that the disease did not disappear until the susceptibles had either died or recovered. In the Middle Ages there were many severe outbreaks of plague, but most of the records are indefinite until the coming of the dread Black Death of 1347–8, which was at first pneumonic and later highly virulent and infectious bubonic plague.

The Black Death arose in the Far East, was carried to Southern Russia by Tatars, devastated Russia, and reached Messina in October, 1347. After spreading over Sicily, it was conveyed to Italy and thence to Southern France in 1348. From France it spread into England, Ireland, the Netherlands, and Germany. Both the incidence and the mortality were terrible. The population of England was reduced from four to two million. There was almost universal panic; the sick and dying were often deserted by doctors and relatives; and desolation and misery prevailed. There were other tragic effects of this widespread pestilence. Unfortunate people were accused of spreading the plague, tortured, and put to death. The Jews were the special victims of this unreasoning panic. Mental disorders occurred. There was the "dance mania," the disease of St. John or St. Vitus, in Germany and Belgium, which later in Italy was known as the *tarantella.*

There were frequent outbreaks of plague in Tudor and Stuart times, the last great one being the Great Plague of London. Singer* has pointed out that in the course of the seventeenth century natural causes were first assigned for the disease, and it was even suggested that it was due to the multiplication of minute organisms, a hypothesis not verified for 200 years. Since then England has been subject to occasional importations of plague, but these outbreaks have been rapidly controlled. Plague prevailed in the Near East during the eighteenth and early nineteenth centuries. At times it spread to Europe. In 1709 there was a big epidemic in Russia, while the famous outbreak at Marseilles and Toulon in 1720 had an excessive mortality. Quarantine and plague hospitals kept the disease within bounds. The Marseilles epidemic and the possible threat of spread to England evoked the *Short Discourse concerning Pestilential Contagion* of Richard Mead, which advanced knowledge of plague and its control by quarantine. In the nineteenth century Sir John Simon organized careful studies of plague, and his valuable series of *Annual Reports* to the Privy Council, extending over thirty years, show how scientific opinion on the cause of epidemic diseases progressed from the conception of a miasma emanating from putrefying filth to a specific chemical poison in air and water, and, finally, to the modern view that specific infections are due to invasion of the body by specific micro-organisms. Hence the study of plague has had an important share in the evolution of epidemiology generally.

In 1894 Kitasato and Yersin independently discovered the bacillus of plague, *Pasteurella pestis*; and P. L. Simond in 1898 showed first that bubonic plague was primarily a disease of rats spread by rat fleas. Much modern research has subsequently been done on this matter, and on the transmission, prevention, treatment, epidemiology, and international and national control of plague.

On all these important aspects, Dr. L. Fabian Hirst, the author of this book, can speak with authority. During a period of twenty-two years he has devoted special attention to plague, and, in addition to an admirable historical and general review of the disease, he now gives mankind the fruits of his researches and experience. The book is well produced, admirably illustrated, and well documented. Those who stay at home will read it for its epidemiological and historical interest, and every medical practitioner engaged in plague work should give it pride of place in the books he consults.

ARTHUR S. MACNALTY.

*"The Black Death and Other Plagues," in *Universal History of the World,* vol. 5.

E.N.T. TEXTBOOK

Logan Turner's Diseases of the Nose, Throat, and Ear. Edited by Douglas Guthrie, assisted by J. P. Stewart, with the collaboration of C. E. Scott, A. B. Smith, I. M. Farquharson, I. Simson Hall, R. B. Lumsden, and J. F. Birrell. Fifth edition, completely revised. (Pp. 468; 246 illustrations and 9 coloured plates. £2 2s.) Bristol: John Wright and Sons. 1952.

This Edinburgh textbook is now edited by Douglas Guthrie assisted by J. P. Stewart and six colleagues. It has been completely revised and brought up to date, and will no doubt hold the same important place as its predecessors; its binding and format are similar. It is divided into seven sections: I and II are devoted to the nose and its sinuses, III to the pharynx and nasopharynx, IV to the larynx, V to endoscopy, and VI to the ear. Section VII is on chemotherapy and antibiotics; since these agents have completely changed the picture of E.N.T. work, it would be reasonable to give them precedence. All sections give considerable space to anatomy and physiology, with excellent illustrations. As students at least have spent time in mastering these subjects, they might well be reduced to a minimum. An exception must be made of physiology of the ear, since the testing of hearing is so closely bound up with it. Generally, the work has achieved a high standard, but the sections on the larynx and the ear must be given extra marks. Both show the wide experience of the authors, and the ingenious use of an attenuated R and L to represent the vocal cords for the instruction of students in the use of the laryngeal mirror might well be generally adopted. The section on the ear is very good and is enhanced by an admirable collection of reproductions of microscopical sections of the temporal bone. The difficult testing for deafness in young children is fully discussed, as is the fitting of hearing-aids. The section on endoscopy gives accounts of the technique of local analgesia for bronchoscopy and oesophagoscopy and removal of foreign bodies, and is well illustrated with radiographs. Most of the 246 illustrations are first-rate, and the nine coloured plates show the lesions well, though the colour is often false.

So much of the subject-matter is admirably sensible that some statements jar, and it is certain that the early authors would not have wished to perpetuate opinions that are no longer valid—for example, "vomerine spurs cause headache," "acute antral infection may lead to swelling of the cheek and oedema of the lower eyelid," in the treatment of an attack of laryngismus stridulus "throw open the window," hypertrophy of the tonsils of such a degree as to produce "difficulty in breathing and swallowing"; and in the instruction of students the dose of calomel should be rather more

specific than "a few grains." However, these are small points at which to cavil and do not detract from the value of this well-established work to students and aspiring specialists.

W. M. MOLLISON.

NEW MEDICAL DICTIONARY

The Faber Medical Dictionary. Edited by Sir Cecil Wakeley, Bt. (Pp. 471. £2 5s.) London: Faber and Faber. 1953.

America has long led the field in medical lexicography, and it is pleasant for a change to see a substantial and attractively written medical dictionary produced in England. This work will be useful not only to doctors but also to nurses, dentists, medical auxiliaries, and administrators and other lay staff of hospitals. Most of the technical devices usual in dictionaries have been dispensed with, and there is a surgical forthrightness about the definitions. The rules for pronunciation are few and simple, and there is no attempt to register variant pronunciations; we can thus continue to pronounce *phthisis* with or without the *ph*, or with the first *s* voiced or not.

It had been hoped to publish the dictionary just after the National Health Service was started, but despite the delay there are understandable defects that can be removed during a leisurely revision. For instance, *pleomorphism* is defined as *pleomorphic state*, but there is no definition of *pleomorphic*; and some much-used words, such as *lymphadenopathy* and *reticulosis*, are not given, but the explanation may well be that nobody knows what they mean. There is, of course, an abundance of exotic terms, and word-fanciers can have a good romp among them. Random samples include *hypurgia* (medical assistance), *rhytodosis* (wrinkling), *lyssa* (rabies), *rhabditis* (a worm, not an inflammation), *hyperphagia* (gluttony), and *stomachalgia* (belly-ache). And with the help of an accountant we can steer safely between the Scylla of *pleonexia* and the Charybdis of *doromania*. At the other extreme we find definitions of many familiar words, such as *belch, belly, bedpan, lust, wine, doctor,* and *patient*, all of which mean what everyone thinks they do; but the fixing of the threshold for words of this type may be difficult.

There are clearly vast numbers of unnecessary words in the medical vocabulary—unnecessary, at any rate, to good medical writers, who know that by taking pains they can make ordinary English do most of the work. We wish the dictionary good luck, and hope that grateful users will help the editor by pointing out errors or omissions.

RAYMOND WHITEHEAD.

REVIEW OF MEDICINE

Annual Review of Medicine. Volume 4. Editor, Windsor C. Cutting; Associate Editor, Henry W. Newman. (Pp. 452. $6.) Stanford, California: Annual Reviews, Inc. 1953.

The Tower of Babel, the vast number of journals, and the writing of papers of which there is no end have made it impossible for the most diligent doctor to keep himself familiar with the literature, even in the small corner of medicine in which he may happen to be particularly interested—much less with internal medicine as a whole. Already most of us have come to rely on abstracts, annual reviews, and articles on recent advances to keep ourselves *au fait* with the aspects of medicine outside our immediate purview. It may well be that in the future original articles will be read largely by specialists and that ordinary doctors will be vicariously nourished by their concentrated ruminations.

The 1953 *Annual Review of Medicine* edited from the Stanford University School of Medicine with the help of a distinguished committee comprises an admirable digest of many hundreds of papers published in the past year. Nineteen authors chew the cud for us. To give the volume an international flavour they include D. P. Cuthbertson, from Aberdeen, who writes on nutrition, and Sir Lionel Whitby, from Cambridge, who writes on diseases of the reticuloendothelial system and haematology. It is surprising that there is no section on endocrinology, in which subject recent advances have perhaps been most prolific and exciting. While general headings such as infectious diseases or cardiovascular diseases are preserved for the sake of orientation and to indicate a framework, an entirely comprehensive survey has not been attempted. Each author has been encouraged to make a thoughtful presentation of those subjects in which he is most interested and to include a few concise paragraphs in which he reflects on other portions of the field. It is all very well done, but in spite of the fact that the publication is non-profit making it is very much more expensive than equivalent British compilations.

D. M. DUNLOP.

ADAPTATION TO ILLNESS

Patients are People: A Medical-Social Approach to Prolonged Illness. By Minna Field. (Pp. 244. 24s.) New York: Columbia University Press. London: Geoffrey Cumberlege. 1953.

The author of this book derives her experience from working in the division of social medicine at the Montefiore Hospital, New York, which is devoted to the study and treatment of prolonged illness apart from mental conditions. It must be admitted that the interest of the physician in the patient suffering from chronic and often incurable disease tends to flag. Such a change is quickly sensed by the patient, to whom the prospect of months or years of illness can be made tolerable only if he feels that those in whose charge he is can and will enter into his fears and problems and help him and his family to the necessary adjustment.

Mrs. Field lucidly discusses the extent of the problem, the ravages of prolonged illness, and the profound mental and social adaptation required to support stay in hospital. The art of learning to live with an illness, to look it in the face as it were, has to be inculcated in these sufferers if they are to be spared the horror of abandoned hopes, which is soon followed by their discharging themselves and bringing further misery to the family.

The hoary question whether a patient should be told the truth about his cancer is discussed—rather, it seems, on the assumption that he will see through the most determined attempt to deceive him. The author's solution appears to be evasive rather than bluntly open in approach, and it is arguable whether in the long run this would be an improvement on older methods. The trouble is that in hospital there are so many people who know the truth about a patient that someone is sure to "let the cat out of the bag." The staff of a hospital for chronic sick cannot, therefore, use the well-tried and usually successful deliberate lie with which countless general practitioners have spared their dying patients the unpleasant truth.

The help of the social worker has been too little publicized in the past, and Mrs. Field's book is to be welcomed as a thoughtful and masterly contribution to the subject.

A. H. DOUTHWAITE.

As a guide to parents in the upbringing of their children, *The Spiritual Development of The Child*, by Dr. Agatha H. Bowley and the Rev. M. Townroe, should help them to provide the "secure ethical and religious background" that Professor A. Moncrieff refers to in a foreword. Written by a children's psychologist and a parish priest, the book covers many of the psychological and spiritual problems that are apt to disturb the growing child. Often enough the problems are one and the same seen in a different light, for, as the authors say, "moral education of the child is intimately bound up with emotional education." The book is published by E. & S. Livingstone for 6s.

The new edition of the *Hospitals Year Book* for 1953–4 is on much the same lines as the previous edition but omits detailed bed and patient statistics for each hospital, since most of these are now made available by the Ministry of Health. Information given for the first time includes details of mass radiography units and of the hospital service in the Isle of Man. The editor, Mr. J. F. Milne, surveys the achievements of the National Health Service over the last five years and points out that the increase in the hospital service's budget has done no more than offset the fall in the value of money. He comments also on the lack of an adequate system of accounting, which is now to be investigated by a Government committee. The book is indispensable to anyone concerned with hospital administration. It is published by the Institute of Hospital Administrators at 2 guineas.

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MALARIA IN EX-SERVICEMEN

The variable signs and symptoms of malaria, with consequent difficulties in diagnosis, have been the subject of many observations in the past. It is therefore not surprising that malaria should have been overlooked in a proportion of those falling ill with it after returning from service in Korea. Some of these men have been ill for a long time, and it is fortunate that the form of malaria prevalent in Korea is not one which causes cerebral or other possibly fatal complications. This, however, is not true of the malaria which may be contracted in tropical Africa or Malaya, where large numbers of British troops are now stationed, and it is important that the possibility of some of them developing malignant tertian malaria should not be overlooked on their return to this country. In our correspondence columns this week Sir Neil Hamilton Fairley gives a timely warning about this. In Africa and Malaya *Plasmodium falciparum* infections are common, and the clinical manifestations of these are even more protean than are those of *P. vivax* and its Korean strain. In neglected cases of falciparum malaria cerebral complications may occur, and if the wrong treatment is given blackwater fever may result.

Among the difficulties of diagnosis is the tendency for the rigor, so characteristic of established vivax malaria, to be less marked in falciparum infections and for the febrile episodes to be irregular though often prolonged. Thus patients may complain only of fever. Others, particularly those with chronic infections, may be afebrile, and though parasites are to be found in their blood they complain of nothing other than vague ill-health. The disease may also present with gastro-intestinal symptoms, jaundice, haemolytic anaemia, or skin petechiae. Cerebral forms may occur with or without hyperpyrexia, and this type of malaria may be confused with cerebrospinal meningitis, epilepsy, acute mania, or alcoholism.

The management of the majority of these ex-Service patients falls in the first instance to the general practitioner, who will make the correct diagnosis much more easily if he keeps in mind the possibility of malarial infection. Knowledge of the patient's recent movements and place of residence is essential. There is much to be said for making such an inquiry more often in taking a history: light might be thrown on a number of diagnostic problems, malarial and non-malarial, if this information was sought as a routine. Sir Neil Fairley's insistence on blood slides being taken before treatment is instituted will be acclaimed by most of those who have followed the correspondence on this subject in recent issues of this *Journal*. Tropical medicine has suffered far too long from the advocates of empirical methods of treatment. It may sometimes be necessary—though it is never desirable—to institute treatment before the films are examined, but it is not justifiable to conclude that malaria caused the fever in the absence of positive blood findings even if resolution of fever follows antimalarial treatment. Therapeutic diagnoses of this kind are full of innumerable pitfalls: the practice may in certain circumstances be a method of handling patients, it is not a method of diagnosis.

P. falciparum parasites are readily eradicated by efficient treatment, and once such treatment has been given there is no tendency for relapses to occur as there is in *P. vivax* infections. Those who have taken prophylactics such as proguanil, chloroquine, mepacrine, or pyrimethamine in adequate dosage and for ten days after leaving the endemic area will not suffer from *P. falciparum* malaria. The danger is to those who have taken these drugs only irregularly or not at all, or who have taken quinine as a prophylactic. Quinine is not completely efficient for this purpose and its use may engender chronic, latent, or recrudescing infections in the presence of which blackwater fever is liable to develop. It is not to be expected that falciparum malaria will be seen on anything like the scale on which vivax malaria has been seen in soldiers returning from Korea. But in view of the greater risks to life and health associated with falciparum infections it is to be hoped that Sir Neil Fairley's warning will not be disregarded.

SMOG MASKS

A cheap and efficient mask giving full protection against such a smog as befell London last winter has yet to be designed, and designers have a difficult task ahead of them. Even so, the two types of mask that regulations made this week allow to be prescribed under the Health Service will probably give some relief to sufferers from chest complaints. Such protection as they may provide would seem to depend mainly on their power to filter off some of the solid particles and droplets in the fog, and the type with a malleable wire frame is likely to be much the more effectual, albeit more expensive. But neither would seem to put much of a barrier against the sulphur dioxide that is believed to constitute the main danger or against any other gases.

Natural fog consists of small droplets, mainly of water, up to about 100 μ in size. Smog contains, besides sulphur dioxide and ash particles, sulphuric acid and particles of tarry distillate. Internal combustion engines, which so far seem to have escaped some of the blame that may well be theirs, emit fine carbon particles and oil droplets, carbon monoxide and carbon dioxide, and traces of lead. The amount of carbon monoxide emitted from motor-cars has recently been estimated at 2,000 tons a day in greater London.[1] Smoke pouring from domestic chimneys is such an obvious contributor to the smog pall that critics of it have been apt to overlook the dangers of the gases given off when smokeless fuels are burnt. Such fuels are not the complete solution to the problem, for they give off sulphur dioxide and carbon monoxide. They are moreover expensive, apt to become scarce when wanted, and unpopular with people who like open fires. Yet the creation of smokeless zones, as we emphasized recently,[2] is probably the best preventive measure that can be undertaken now, even though the oxides of sulphur may not be much diminished in such zones; and it is gratifying to note that London is following the lead given by Manchester and Coventry in establishing one. As Professor Drinker pointed out in a lecture at the London School of Hygiene last April, we have legal specifications governing the purity of water, milk, food, and drugs: why not of the air?

While nothing more than strong suspicion has yet fallen on the oxides of sulphur as the chief menace in smog, evidence has been provided by Professor Drinker and his colleagues[3] that healthy adults experience shallower and more rapid respiration and an increased pulse rate after breathing sulphur dioxide for 10 minutes at a concentration of 1 p.p.m., the effects being more severe with increase of concentration. During the smog last year the maximum concentration of sulphur dioxide was rather over 1 p.p.m. in central London, and the mean was about 0.9 p.p.m. during December 5–9. Healthy adults, however, were not gravely affected: it was those with disease of the heart and lungs who succumbed so quickly,[4] and the exact cause of their death is not yet known.

Though catastrophes like last winter's are rare, research into its circumstances is urgently needed and into the preventive efficacy of masks against both particles and gases. The Ministry's masks will be of some value, and the London Local Medical Committee has performed a useful service in rousing medical and public opinion about the dangers of smog to certain persons,[5] apart from its general nuisance to everyone. But neither type of mask contains any chemical, for instance, to neutralize or adsorb the gases that are believed to be more harmful than the particles. No doubt we shall soon be informed of results of testing masks impregnated with some alkali such as sodium carbonate, or containing charcoal granules, or made of one of the special fabrics formerly developed in research on chemical warfare. Apart from all this, patients with cardiac or respiratory disease, in special need of protection, may experience difficulty in breathing when wearing masks. Some patients, though not suffering from bronchospasm, may yet develop it if they put on a mask, either for psychological reasons or because of the increased resistance to breathing. Neither the medical profession nor the public should be lulled into a false sense of security by the rather rapid decision to issue masks. In fact, Mr. Macleod admitted in the House of Commons on November 3[6] that further research was needed before determining what type of mask could be safely worn by those in special need of protection against smog. We need more facts, and it is much to be hoped that investigations will proceed apace, for last winter's smog was directly responsible for some thousands of deaths.[1 4 7]

1 Wilkins, E. T., address delivered at Royal Sanitary Institute on November 11, 1953.
2 *British Medical Journal*, 1953, **2**, 818.
3 Amdur, M. O., *et al.*, *Lancet*, 1953, **2**, 758.
4 Martin, W. J., *Med. Offr*, 1953, **90**, 233.
5 *British Medical Journal*, 1953, **2**, 1055.
6 Ibid., 1953, **2**, 1108.
7 Logan, W. P. D., *Lancet*, 1953, **1**, 336.

TOWARDS CLEANER FOOD

Although the Food and Drugs Amendment Bill which was introduced in the House of Lords on November 10 may be popularly known as the "Clean Food Bill," it is concerned with other matters besides food hygiene. For instance, the Bill prohibits the sale of food made injurious to health by "addition, abstraction, or other process." Other chemicals besides preservatives are now commonly used in the manufacture of food, and some of these may be harmful in their cumulative if not in their immediate effect. The Bill gives power to the Minister of Food to obtain full information from the manufacturers about any new substances which are intended for use in the preparation of food, including information about any investigations which may have been made into the harmfulness or otherwise of the substances concerned. Clause 3 of the Bill gives the Ministers of Food and of Health wide powers to control the composition of food and its method of manufacture. Under these powers the Minister could make regulations prohibiting the use of certain substances in the preparation of food—a wise provision in view of present trends in food

manufacture. The Ministers are also to be given powers to regulate the labelling and advertising of food. Under a Defence Regulation it is already an offence for a manufacturer to make misleading claims about the nutritional value of a food either on labels or in advertisements, and the Bill puts this legislation on a permanent footing.

Section 13 of the Food and Drugs Act, 1938, contained specific provisions about the sanitary condition of premises used for the preparation of food. If these provisions were intended to prevent outbreaks of food-poisoning they cannot be said to have been very successful, though it is only fair to point out that in 1938 no one had any idea that communal feeding would become so important in the life of the nation as it has done. In the new Bill this section is repealed and the Ministers of Food and of Health are given power to make regulations covering the whole field of food hygiene, including the construction, equipment, and cleanliness of premises, the use of materials, the manufacture of apparatus for the preparation of food, and the inspection of meat. Under existing regulations premises used for the manufacture or sale of sausages, ice-cream, and preserved foods have to be registered by local authorities, and the Bill proposes to extend registration to food businesses of all kinds. Clause 9 empowers the Ministers to make regulations requiring the owners of stalls and barrows on which food is offered for sale to obtain a licence from the local authority.

This Bill centralizes power in the hands of the Ministers of Food and of Health and continues a trend of rule by regulation which is deservedly unpopular, but it may be welcomed as showing the Government's intention of coming to grips with a serious health problem. The provisions of the Bill can be no more than the groundwork on which to base a campaign for safe and clean food, and it is to be hoped that local authorities will take their responsibilities more seriously than many of them have done in the past. But in the long run the success of the plans to make dirty food a thing of the past will depend on the public. The "education" of food manufacturers and handlers will be painfully slow if the public remain apathetic about the purity and cleanliness of the food they buy in shops, canteens, cafés, or restaurants. How many people complain when they see their butcher digging his hands into a bowl of mince or their confectioner using her fingers to pick the chocolates out of a box?

Some critics of clean-food legislation point out that the very people who complain most about dirty food in this country will go into raptures about the deliciousness of meals cooked in Continental kitchens which even by existing British standards would certainly be condemned. But in such places the customers at any rate can relish the food, prepared as it is with a genuine appreciation of its quality and appearance. Food which is picked over by unclean hands and mutilated in its manufacture, cooking, storing, and serving is unsavoury as well as unsafe, and the public should exercise their discrimination and support only those concerns—and fortunately their number is steadily growing—which give food the respect it deserves in a civilized country. One day perhaps it will no longer be considered overrefined to feel squeamish about eating a meal among the litter and slops of a previous customer.

TREATMENT WITH ANTIBIOTICS

We print in the opening pages of this issue the general introductory paper contributed by Dr. Maxwell Finland at the Antibiotics Symposium in Washington, an account of which was given in the *Journal* a fortnight ago.[1] Dr. Finland has been one of the foremost clinical investigators in the field of bacterial chemotherapy since the days when our only resources were the sulphonamides. With his collaborators in the Thorndike Memorial Laboratory at the Boston City Hospital he has also been responsible for extensive laboratory studies of the kind on which the intelligent direction of such treatment must often depend. Further, he has had the earliest opportunities of conducting clinical trials of antibiotics still unfamiliar or even unknown in this country. Thus he can already express opinions on the merits of erythromycin and carbomycin, and has had sufficient experience with tetracycline to be able to affirm not only its therapeutic utility but the relative freedom from gastro-intestinal side-effects enjoyed by patients treated with this drug.

His pronouncements on more general questions, and on the use of the older antibiotics, will also command respect. A frequently recurring theme in his paper is the danger of indiscriminate use; it even seems, in the light of American experience, that the scarcity of some antibiotics in Britain and the restrictions placed on their supply may be a positive advantage. At least it can rarely be possible here to treat a patient with "four or even six antimicrobials at one and the same time." It is also interesting to read that new antibiotics are coming into general use before their properties have been adequately studied—a quite unfamiliar situation to us. A good deal of space is rightly given to the proper use of penicillin, the indications for aqueous and repository forms respectively being defined: oral administration is considered to be of limited usefulness, and the superiority of some new forms of this drug for which special properties are claimed is regarded as unproved. Dr. Finland defines the indications for streptomycin in infections other than tuberculous, and suggests a policy for the use of this drug and dihydrostreptomycin with a view to avoiding serious eighth nerve damage. In the discussion of chloramphenicol promi-

[1] *British Medical Journal*, 1953, **2**, 1043 and 1035.

nence is naturally given to the question of its toxicity: on this the author takes a moderate view, but he points out that a warning of approaching marrow aplasia may not be obtainable by serial blood counts during the actual course of treatment. It is interesting that doubt should be cast on the efficacy of this drug in salmonella infections other than typhoid fever: another slightly iconoclastic feature is the author's scepticism about the usefulness of the tetracyclines in virus diseases.

The prediction that meningococcal infection will increase in prevalence is interesting, and the warning against initiating the treatment of cerebrospinal fever with procaine penicillin will probably be new to most readers: sulphadiazine is still considered to be the drug of choice for this disease. Perhaps the fullest discussion of all is devoted to the subject of prophylaxis, of which five types are first defined, according to the object in view. The necessity of defining the precise object is emphasized in connexion with antibiotic cover for dental extractions, and the observations on this are an interesting commentary on recent correspondence in this *Journal*. It is a very good rule, as suggested here—although not always easily carried out—to use for prophylaxis some other drug than that which will be indicated for the treatment of subsequent infection, should it occur.

APPENDICITIS IN THE YOUNG CHILD

The returns of the Registrar-General show a steady and reassuring fall in the total number of deaths each year from acute appendicitis. It is, however, a disconcerting fact that there has been during the past twenty years no improvement in the mortality figures under the age of 5. In 1930, out of a total of close on 3,000 deaths from appendicitis, 130 children under 5 died from this cause, while in 1950 the comparable figures were 142 deaths out of a total of only 1,300. This state of affairs would be easy to understand if the disease was especially common in the first years of life, but this is by no means the case. On the other hand, surgeons have found at operation that acute appendicitis in infancy and early childhood is complicated by peritonitis or by abscess formation in a percentage which varies between 40 and 60.[1 2] As would be expected from experience in the treatment of adults, the overall mortality rate is correspondingly high. It seems further to be true that the very young are particularly vulnerable to acute peritoneal inflammation. Ladd and Gross[3] reported a mortality rate from peritonitis following appendicitis of 11% under 4 years as compared with only 1.6% in children above that age.

Anatomical facts such as the large amount of lymphoid tissue in the infant's appendix, and the relative maldevelopment of the omentum at that age, may help to explain not only the occurrence of early perforation of the appendix but also the lethal infection which may then ensue, but it is delay in making the diagnosis that is most often responsible for the high fatality rate. The percentage of cases with rupture of the appendix will rise with every hour that passes: when the symptoms have been present for more than 24 hours roughly 1 in 3 will already have perforated.[3] For delays and errors in diagnosis there are many good reasons: they were evident in Bunton's[1] analysis of 115 consecutive unselected cases operated on in the Westminster Children's Hospital. Although we think first of appendicitis when we are confronted with an adult, previously healthy, who complains of acute abdominal pain and vomiting, this diagnosis is less likely to suggest itself in the infant, largely because it is widely held to be uncommon in the early years of life. Experience has shown, however, that in any large children's hospital as many as 25 to 35% of cases of acute appendicitis occur below the age of 5.[1] Further, although the classical sequence of pain, vomiting, tenderness, and rigidity and fever may make the diagnosis easy, the history in early childhood is often misleading. Vomiting is a more constant feature than pain[4] and seems not uncommonly to come first. The pain which abates after perforation may disarm suspicion. Perhaps most misleading of all is the frequency of diarrhoea[1 4]: the combination of abdominal pain and diarrhoea, with some tenderness and fever, all too closely mimics gastro-enteritis and occasions tragic delay. The almost inevitable course of antibiotics that follows may still further confuse the diagnosis.

Every practitioner is acutely aware of the difficulties of abdominal examination in the young child. The most patient and painstaking handling is imperative. Tenderness and rigidity are seldom absent, but they may be found only low down above the pubis or high up just below the rib margin. But the diagnosis is certainly not easy in the early stages. As Bunton wisely says, "The only real safeguard is unceasing vigilance." Careful surgery, aided by antibiotics, can save these children when they come to operation early, but, so long as there is delay in establishing the diagnosis, so will the recovery rate in the young lag far behind the much more encouraging figures in the adult.

NOCTURNAL MYOCLONUS

Sudden involuntary jerks of the limbs, often called myoclonic jerks, are common in patients suffering from idiopathic epilepsy, and sometimes they increase in frequency for a day or two before a major convulsion. These jerks are usually most common first thing in the morning. Symonds[5] has recently considered the problem of myoclonus occurring as a patient is dropping off to sleep—nocturnal myoclonus. In this condition, when the patient begins to doze sudden involuntary jerks occur. They are chiefly in the legs, but the arms too may jerk, and at times there is involuntary contraction of the respiratory muscles. Consciousness is unimpaired, and as a result of the involuntary movements the patient wakes up. While he remains awake

[1] Bunton, G. L., *British Medical Journal*, 1953, **2**, 71.
[2] Packard, G. B., and McLaughlin, C. H., *J. Pediat.*, 1951, **39**, 708.
[3] *Abdominal Surgery of Infancy and Childhood*, 1951, Philadelphia.
[4] Williams, H., *British Medical Journal*, 1947, **2**, 730.
[5] Symonds, C. P., *J. Neurol. Neurosurg. Psychiat.*, 1953, **16**, 166.
[6] Muskens, L. J. J., *Epilepsy*. London. 1928.
[7] Hodskins, M. B., and Yakovlev, P. I., *Amer. J. Psychiat.*, 1930, **86**, 827.

there is no myoclonus, but when he dozes he is again awakened by the involuntary movements; this sequence may occur repeatedly throughout the night and seriously interfere with sleep. Symonds suggests that this type of myoclonus also is an epileptic phenomenon, and he gives five case histories. In one, epileptic attacks had occurred in the past; a second patient had had a vasovagal attack of the type described by Gowers; and two of the others had had head injuries of some severity but had no evidence of epilepsy. The electroencephalogram was normal in two patients, in a third was abnormal, suggesting a diffuse or basal lesion but without evidence of epileptic activity, and it was not recorded in the other two patients. In one patient there was a good response of the nocturnal myoclonus to administration of troxidone, but this drug had been ineffective in a second case. Nocturnal myoclonus of this type has previously been described in known epileptics,[6 7] and, though the evidence is not conclusive, there are reasonable grounds for considering this rather rare and incommoding symptom to be epileptic and for administering anti-epileptic drugs.

Symonds has also raised a much more controversial problem—the relationship to epilepsy of that common symptom, a single sudden jerk of the legs when the subject is fully relaxed in bed and just dropping off to sleep. He states that for many years he has suspected that the liability to nocturnal jerks of this type, if excessive, may be associated sooner or later with the manifestation of epilepsy. Perhaps fortunately for the peace of mind of many of his readers he has not defined the word "excessive." He has over the years inquired about the liability to such jerks in patients who later develop epilepsy; in some this excessive liability has been noted, and in a few a similar liability has been present in near relations, though they have never had overt epileptic attacks.

A NEW DRUG

Last year a substance ("4560 R.P.") was described[1] by French authors as a new stabilizer of the autonomic system. Its formula showed it to be a very slightly modified form of promethazine ("phenergan"), with a similar toxicity but with some remarkable properties. It was said not to be an antihistamine, as might have been expected, but to be a ganglion-blocking agent like hexamethonium, to be similar in action to diethazine ("diparcol"), and also to be a sympatholytic—that is to say, an anti-adrenaline compound—to prevent vomiting, and to reduce temperature. When given in a 50-mg. dose together with 100 mg. of pethidine it was stated to enhance the analgesic action of pethidine to such a point that only a minimal amount of volatile anaesthetic was necessary to produce excellent surgical anaesthesia. The authors also used it to augment the effect of an intravenous infusion of procaine amide; the procaine amide alone had no effect on wakefulness and little action on blood pressure, but together with 4560 R.P. it produced a vascular paralysis going so far as a disappearance of the radial pulse. The substance was said to have a curarizing action and, finally, to potentiate the barbiturates. After previous administration of a combination of morphine, atropine, and promethazine, the slow intravenous injection of 50 mg. of 4560 R.P. and 100 mg. of pethidine was enough to make intubation possible.

At a recent European congress this compound received a good deal of publicity, and one may reasonably ask on what evidence the claims in its favour are based. Since 4560 R.P. resembles promethazine so closely in its constitution, the authors of the paper cited might have been expected to establish that it was different from promethazine by incontrovertible evidence. Statements that 4560 R.P. will potentiate the action of pethidine and of barbiturates can easily be verified by animal experiment. Yet no trials of this kind have been published either to establish a potentiating action or to show that 4560 R.P. possessed such an action to a greater extent than promethazine. Similarly statements that the substance 4560 R.P. is a ganglion-blocking agent might be expected to be supported by animal experiment. Tests for this property are simple enough to be carried out by medical students in a practical class.

Another property claimed for this substance is that of producing what is dramatically called artificial hibernation—in other words, to cause a fall of body temperature—and according to a recent report[2] this effect of the drug is found useful in such diverse conditions as normal midwifery and cerebral haemorrhage in premature infants. In 1948 Dutta[3] showed that many substances such as pethidine, atropine, the antihistamine "benadryl" (diphenhydramine hydrochloride), procaine, and quinidine all possessed this property; and in the following year he reported[4] that they have some curarizing action, some ganglion-blocking action, some local anaesthetic action, and some quinidine-like action on heart muscle. Thus the substance 4560 R.P. appears to be another member of a large group of substances which have many properties in common. On the important question whether it possesses some of these properties in outstanding degree no comparative evidence of any sort has been offered.

Recently under a new number (compound 2601-A) the same substance has been described[5] in the U.S.A. as a new anti-emetic agent, of value in suppressing nausea and vomiting due to the administration of drugs such as disulphiram ("antabus") plus alcohol, aureomycin, morphine, and several others. No quantitative comparison with any other remedy for vomiting was described, and there seems no reason to suppose that the same effects would not have been obtained with promethazine. When there has been so much discussion of the relative value of different drugs for preventing sickness it is surprising to read an account of this sort, since it is usual for commercial firms introducing new compounds, and for medical men publishing results obtained with them, to study the pharmacological action of the group of substances to which the compound belongs and to carry out clinical trials only when a full investigation of effects on animals has been made.

[1] Laborit, H., Huguenard, P., and Aulluaume, R., *Presse méd.*, 1952, **60**, 206.
[2] *Lancet*, 1953 **2** 1039.
[3] *Brit. J. Pharmacol.*, 1948, **3**, 246.
[4] Ibid., 1949, **4**, 197.
[5] Friend, D. G., and Cummins, J. F., *J. Amer. med. Ass.*, 1953, **153**, 480.

CLINICAL PATHOLOGY IN GENERAL PRACTICE

THE COLLECTION OF FORENSIC SPECIMENS

BY

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A great responsibility rests upon the practitioner, be he in clinical or pathological practice, who is called upon to make an examination and obtain material which may be of use in a court of law. However few or many the specimens he may see fit to take, there are certain guiding principles to observe. He should take the specimens himself and see that they are properly labelled and sealed; he should obtain a receipt from the officer or laboratory to whom they are handed; and he should remember that there is no time like the present, since in most forensic cases "the present" may be the only opportunity for obtaining specimens of real value.

Guiding Principles

The first principle should not need to be accentuated in our profession, but, despite the strictest precautions, bottles of blood for transfusion, cylinders of gas for anaesthesia, not to mention ampoules of drugs for injection, are still confused, with fatal results; and, while it is bad enough to have such a disaster on one's hands when the patient is perhaps unlikely to live in any event, it is even worse that a criminal should escape justice or an innocent man be convicted as the result of carelessness or inaccuracy in a simple procedure. Cases have occurred in which a doctor has been unable to identify his own specimen bottles and slides when confronted with them in the witness-box, and it should be stressed that all samples must be so adequately labelled as to be identifiable to all parties subsequently. Samples should whenever possible be taken in glass containers, and these should be sealed with an adhesive tape such as "selotape." Sealing-wax has largely gone out of fashion because of its uncertain chemical constitution; if used, it should be applied only to the outside of the adhesive tape and not to the lid of the container. Slides can be conveniently transported in small wooden slide-boxes, which again should be sealed with adhesive tape. If such boxes are not available, corrugated brown wrapping-paper, cut to shape, rolled, and sealed, makes a good alternative.

The importance of continuity of identification of specimens is the reason for the second principle. It is convenient, incidentally, to have the receipted list of specimens readily available when giving evidence in court. This may save considerable embarrassment when being questioned on what specimens were actually taken, since it is not always easy to remember under the stress of cross-examination a list of, say, 10 or 12 samples, some of which may not have seemed particularly important when they were obtained.

With regard to the third principle, while an attempt will be made to point out the material which should be collected on the spot, it must be remembered that there are rarely two homicides completely alike, and that it is better to take too many specimens rather than too few. In particular, beware of the police officer who says, "I'm not keen on all this scientific stuff, Doctor. I want straightforward facts to put before the jury which they will understand." He will ring you up a week later to tell you that his superintendent or the Director of Public Prosecutions now wishes to have a sample of X or Y or a photograph of bruise Z. In this connexion it is worth stressing that the doctor should never hesitate (for fear his original thoroughness be doubted) to have a second or third look at a body. It is surprising how bruises and abrasions show up or fall into a pattern once a body has been exsanguinated by post-mortem examination. Similarly, in cases of alleged rape bruises which are not apparent at examination shortly after the incident may come up during the next 24 hours, and be easily seen if the patient is examined again.

In forensic cases it is essential to have permission from the person concerned (and from his or her guardian if the person is under 21), not only before any specimens are collected but before any examination other than simple observation is made. This permission should be obtained in writing.

The chief problems which will concern the general practitioner, or more particularly the police surgeon, are those associated with the examination of motorists alleged to be under the influence of alcohol or drugs (Section 15 of the Road Traffic Act), cases of rape, buggery, and assault. While the investigations in these cases will naturally differ according to whether the person is alive or dead, it is convenient to consider them in relation to the nature of the charge.

Tests for Alcohol

The clinical examination of the allegedly alcoholic motorist is outside the scope of this article, but in certain county constabularies requests for samples of blood and urine for analysis for alcohol content are becoming more frequent. The importance of obtaining permission before taking such specimens must once again be underlined. The motorist need not subject himself to such examination, but refusal frequently goes against him in subsequent proceedings.

If the police want these tests done they should provide the receptacles for the specimens. In the case of blood alcohols it is most important that the skin should not be cleansed with any material containing alcohol, and the same applies to the syringe. Soap and water are generally considered the best cleansing agents for the skin in these cases, and an 8-ml. oxylated "venule" should be used to collect the blood. It is not the custom in this country to use fluoride in the venule to prevent fermentation, therefore the venule should be either refrigerated or transported immediately to the police laboratory, where it may be divided into two or three equal parts—one to be available to the defence. The speed of transport in this as in any other forensic case is of course the responsibility of the police. Urine should be collected in a clean bottle and filled to the top if possible. In no case should the urine occupy less than one-third of the bottle. The police commonly supply 4- or 6-oz. (100- or 150-ml.) bottles.

Blood alcohols are sometimes of value after death, and may explain circumstances which otherwise would be inexplicable, as in certain traffic accidents and street fights. The blood should be taken from limb veins and not from the heart, as it has been shown that alcohol from a loaded stomach may contaminate the heart blood after death. These samples should, of course, again be taken into containers which have had no contact with alcohol. Again, as a general principle, the amount of blood taken should not occupy less than one-third of the container.

Sexual Assault

The examination of clothing in cases of alleged rape is, generally speaking, the responsibility of the police laboratories. This does not mean to say that the ordinary powers of observation should not be exercised with regard to the

distribution of tears, blood-stains, and stains of semen. The local police force can be expected to provide suitable containers in which the clothing can be placed and which can be sealed. It will be remembered that to substantiate a charge of rape it is not necessary to show complete penetration. Indeed, it has been held in court that the presence of semen within the labia minora is proof of penetration within the meaning of the law. It is therefore important to make a detailed examination of the vulva and vagina—initially swabs should be taken from within the labia and carefully labelled; afterwards they should be taken from higher up the vaginal canal. Under optimum conditions a speculum may be used, but satisfactory smears can generally be obtained without this, on an ordinary throat swab. It has been found, however, that spermatozoa deteriorate fairly rapidly on cotton-wool and it is best to make an immediate smear on a glass slide from the swab and hand both swab and smear to the officer in charge of the case.

In cases of rape, blood-grouping may be necessary, and blood should be taken both in citrate and as whole blood. While citrated blood is more readily available for immediate examination, whole blood is preferable if there is likely to be any delay in the transport of the specimen. In any case of delay the blood specimen should be stored in a refrigerator at a temperature of between 4 and 6° C., but it should not be frozen. While a few drops of blood are, of course, enough for most groupings, it is always advisable to have material to spare, and when practicable 1 ml. or more of blood should be collected and half of it placed in 3.8% sodium citrate solution (four volumes of blood to one of citrate). The blood should be taken into chemically clean bottles, preferably sterile. Samples of pubic hair are also of importance, and as these samples should contain the hair root it is better to pluck the hairs at the end of the examination lest the patient's co-operation be lost at an early stage. The post-mortem examination of cases of suspected rape will be conducted along similar lines but in considerably easier circumstances.

The collection of specimens in cases of buggery will closely follow those described above, but here it is even more important that anal swabs should be immediately smeared on to glass slides and any material of a lubricating nature, such as petroleum jelly or paraffin, should be carefully looked for and preserved. The splashing of semen in the perianal region should also be looked for, and a damp swab will often be sufficient to remove an adequate sample of semen from this region.

Assault

Here the forensic duty of the doctor lies mainly along the lines of detailed and accurate observation of wounds, and it is perhaps only necessary to underline the importance of removing where possible and preserving any foreign bodies such as fragments of glass or metal which may remain in these wounds. To constitute a wound in law the whole skin or mucous membrane must be broken. An abrasion is not sufficient. Paint, metal, or glass adherent to or driven into the body should be preserved. In the majority of these cases it is important to take blood for grouping.

Traffic Accidents

The possibility of contact traces of vehicles in "hit and run" traffic accidents should be remembered. Whether the victim be alive or dead any extraneous fragments of paint, metal, glass, or fibres found adherent to the body or its clothing should be preserved in small bottles or tubes, and, more particularly if the victim is dead, samples of blood and hair taken for comparison with material subsequently found on a suspected vehicle. The preservation of skin showing the imprint of a tyre or radiator is a difficult problem owing to the shrinkage which occurs on removing the skin from the body, quite apart from artifacts and deformities resulting from fixation. Photography is a much more satisfactory method of recording such injuries for future comparison. This applies to any injury involving skin, and the photograph should include a scale to avoid dimensional errors.

Homicide

The material that should be preserved in the case of homicide will naturally vary from case to case, but generally speaking the following samples should be collected: hair, both head and pubic; blood, a large enough sample for both grouping and alcohol estimation; finger-nail scrapings; stomach contents; urine; vaginal and anal swabs; and saliva.

Hairs.—Hairs should always be plucked to include a sample of root, and placed in small well-stoppered bottles or tubes. Envelopes may be used in emergency, but hair is better confined and more easily seen in a glass container.

Blood.—The precautions necessary in the taking of blood for alcohol analysis and blood grouping have already been explained. Blood taken for carbon-monoxide estimation should always fill the container—a 4-ml. screw-capped bottle is entirely adequate. The amount of carbon monoxide lost to the air above the surface of the blood in a partially filled bottle, particularly if it is shaken in transit, may easily amount to 25% of the original content.

Finger-nail Scrapings.—These are generally collected after death. They may be taken by clipping the nails into separate glass tubes or by using sharpened matchsticks to remove the debris from beneath the nails. The latter is considered more effective. Ten matches should be sharpened and two sets of five small glass tubes strapped together with adhesive tape, and labelled "left" and "right" and 1 to 5.

Stomach Contents.—Quite apart from the question of poisoning, the stomach contents should be retained in all cases of homicide, as they are occasionally of value in estimating the time of death. The stomach, having been tied at the cardiac and duodenal ends before removal from the body, should be opened over a wide-mouthed glass container (chemically clean), and after immediate and necessarily superficial examination it should be added to the contents and the container closed by means of a non-metal cap or stopper.

Urine.—This can generally be conveniently collected by manual compression of the bladder into a sterile container. All the urine should be preserved.

Material for Chemical Analysis

In cases of suspected poisoning it is necessary to collect virtually the whole of the intestinal tract with its contents, the liver, the kidneys, a large sample of hair, a sample of bone, and urine. Chemically clean containers should be obtained from the police. The stomach, the small intestine, and the large intestine should be tied off separately and their contents emptied into separate containers before examination of the mucosa. The hair should be plucked, and a long bone removed intact (to avoid contamination with a metal saw). As large a sample of blood as can conveniently be obtained (up to a pint or more—600 ml.) may be of great value in the detection of certain drugs which are not specifically absorbed by solid organs. For instance, the presence of aspirin, the barbiturates, and antihistaminic drugs may often be determined much more easily in a large sample of blood than in any solid organ. In cases of suspected murder by poisoning each organ or type of material should be placed in a separate container.

In post-mortem examinations for coroners in cases of suspected suicide or accidental death, it is generally sufficient to place the solid organs in one container and the organs containing fluids each in separate containers.

In cases of exhumation, samples of soil above, at the side, and below the coffin should be taken separately. The identification of the chemical structure of the coffin and its nails is of course not the responsibility of the doctor.

A copy of the medical practitioner's findings should accompany (or follow as soon as possible) the specimens

to the police laboratory. Generally speaking it is not the duty of the medical practitioner to act in the role of the policeman, but, on the other hand, it is perhaps a waste of time to have taken trouble in the collection of specimens without indicating to the police scientists (who are not usually medically qualified) the reasons for which the specimens were taken. It is therefore reasonable for the medical practitioner to indicate what lines of investigation he thinks necessary on the material he has provided.

In conclusion, it is necessary to stress once again that, unless the samples which have been taken are properly labelled and sealed and delivered with celerity and safety, the trouble and care devoted to their collection will be completely wasted and valueless.

Next article on Clinical Pathology.—"Urine Testing in the Surgery," by Dr. H. E. Archer.

Refresher Course Book.—The first collection of articles in the Refresher Course for General Practitioners (fully revised) are available as a book containing 55 chapters, price 25s. Copies can be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers.

BRITISH ORTHOPAEDIC ASSOCIATION

ANNUAL MEETING

The annual meeting of the British Orthopaedic Association was held at the Queen Elizabeth Hospital, Birmingham, on October 23 and 24. Sir Reginald Watson-Jones was in the chair on the first day, and on the second day he was succeeded by the new president, Professor Bryan McFarland. Clinical meetings were held at the Royal Orthopaedic Hospital, Birmingham, the Birmingham Accident Hospital, and the Rehabilitation Workshop of Austin's factory, and as a new feature an instructional course in orthopaedic surgery was given on the day before the meeting.

Sir REGINALD WATSON-JONES, in his presidential address, reviewed the progress and development of the British Orthopaedic Association. It had created firm ties between the orthopaedic surgeons of Great Britain, the Commonwealth countries, and the United States of America. The British Orthopaedic Association had given strong support to the foundation of the New Zealand Orthopaedic Association and the South African Orthopaedic Association, and, with equal generosity from the United States and Canada, it had secured the foundation of Travelling Fellowships for young orthopaedic surgeons between the United States, Canada, and Britain, with a share by other countries of the Commonwealth.

Mindful of the value of tradition, the association had recently taken steps to stimulate interest in historical treasures relating to orthopaedic and allied subjects. A collection of such treasures had been started, and it would be housed at the Royal College of Surgeons of England, where a selection would always be on view in the College Hall. Among the items of special interest were the percussion hammer used by Hugh Owen Thomas, his flute, his smoking-cap, and the signet ring with which he used to seal the collar-and-cuff slings so that they would not be removed without his knowledge before the next visit.

Judet Arthroplasty

Mr. D. LE VAY (London) gave an account of his experience of replacement arthroplasty with a Judet-type prosthesis as the primary treatment of sub-capital fractures of the neck of the femur. He thought that the method was well justified in the elderly. Most patients had been allowed up 4–5 weeks after the operation and the average length of stay in hospital was 10 weeks. Although there had been a tendency for the head to migrate into a varus position a point of stability was reached beyond which no further displacement occurred.

Mr. O. J. VAUGHAN-JACKSON (London) recalled that at a clinical demonstration at the combined meeting of the orthopaedic associations of the English-speaking world in 1952 he had shown elderly patients with fractures of the neck of the femur treated primarily by replacement arthroplasty. Though privately optimistic, he had at that time adopted a cautious attitude. A further year's observation of these patients and of others in his total series of 34 cases had confirmed him in his optimism, but it was still too early to make a final assessment of the merits of the operation. Its limitation was that at best it did not give a normal joint, which was not true of a successful nailing operation: it could therefore not be recommended for all patients with femoral neck fractures—certainly not for those in their fifties or sixties. Nevertheless he believed that it could be recommended for the really aged, for it avoided the uncertainties of the nailing operation, with the likelihood that a high proportion of patients treated by nailing would require further operative treatment later. Of his 34 cases, the operation was tolerated well in 32 and poorly in 1; 1 patient died. The main local complication was fracture of the prosthesis, which occurred in 4 cases; the use of metal prostheses in place of plastic would probably solve the problem of breakage. Walking was resumed 5–6 weeks after operation. Most patients preferred to use sticks for at least six months, but none complained of severe pain.

Mr. G. N. GOLDEN (Guildford) reported 60 cases of Judet arthroplasty for fracture which he had reviewed in collaboration with Mr. C. C. M. MURRAY (Southsea) and Mr. A. G. ORD (Portsmouth). The results were good in 70% and satisfactory in a further 15%. He agreed that the operation offered advantages over nailing in the aged. Mr. K. H. PRIDIE (Bristol) condemned the operation of primary Judet arthroplasty for fractured femoral neck. In 57% of cases in which treatment was by nailing the hip was indistinguishable from normal. Avascular necrosis was inevitable in 11%, but this was balanced by a 12% incidence of fractured acrylic prosthesis. Judet arthroplasty should be reserved for the treatment of fractures in which nailing had proved unsatisfactory. Dr. J. T. SCALES (Stanmore) said that further work was required on the properties of materials used for internal appliances. Plastics were liable to heat deterioration, but metals were also liable to defects resulting from stress.

Mr. G. K. ROSE (Shrewsbury) spoke on the problem of the "valgus" or "pronated" foot. The dividing line between normal and abnormal was ill-defined, and the indications for treatment and for its cessation were indefinite. He had therefore undertaken a long-term investigation of the feet of 177 children aged between 6 and 8 years. His conclusions were that some valgus shift was normal, but that there was no difference in this between boys and girls. The essential pathological feature in the abnormal valgus foot was strain of the peritalar joint, not simply an abnormal position of the joint.

Causes of Coccydynia

Mr. H. J. RICHARDS (Oswestry) reviewed the possible causes of coccydynia in the light of a study of 102 cases. A history of injury was present in less than half the cases. Infection and neoplasm were occasional causes, but could not explain the majority. Psychogenic factors were secondary rather than primary. He believed that in many cases coccydynia was caused by a central prolapse of one of the lower lumbar intervertebral disks. He supported this hypothesis on theoretical grounds and by clinical observation. Thus 40 out of 1,000 patients diagnosed as having a disk protrusion complained of coccydynia in association with sciatic pain; and nearly half of the patients with coccydynia had low backache or sciatica to begin with and most of the remainder later developed similar symptoms.

Mr. K. I. NISSEN (London) expressed strong disagreement with this hypothesis. In his experience relief from coccydynia could nearly always be assured by repeated manipulation of the coccyx; excision might be necessary in 5–10% of cases. He could not accept the argument that prolapse

of an intervertebral disk played a direct part in the aetiology. Mr. H. K. LUCAS (Bristol) supported the concept of root pressure as a cause of coccygeal pain. Mr. G. K. ROSE (Shrewsbury) had had success with the treatment of coccydynia by plaster jackets.

Mr. J. N. WILSON (Cardiff) reviewed 57 fractures of the lateral condyle of the humerus in children, with particular reference to the complications and treatment. In treatment, conservative methods were usually successful. If the fracture was irreducible or unstable operative reduction was required. After accurate reposition of the displaced fragment fixation was secured by a Pidcock pin. Professor BRYAN MCFARLAND (Liverpool) advocated caution in immobilizing injured elbows in plaster. Discussing the complication of late ulnar palsy, he agreed with Mr. Wilson that it was not caused by deformity alone. He ascribed it to an irregularity of the shape of the medial condyle secondary to the distortion of growth at the lateral side. Mr. O. J. VAUGHAN-JACKSON (London) said that the irregularity might not always be bony; a collection of "pin-head" ganglia could be sufficient to impair the function of the nerve.

Treatment of Peripheral Arterial Disease

Professor F. A. R. STAMMERS (Birmingham) said that there were many points of common interest between orthopaedic surgeons and vascular surgeons. He recalled that sympathectomy was first done for vascular disease by Adson at the Mayo Clinic. It had been done previously for spastic conditions, and it was the observation that the limbs became warmer and drier that led to its trial in vascular disease. The vascular conditions that might be benefited by sympathectomy could be classified under five headings: (1) those from spasm—impaired circulation after poliomyelitis, acrocyanosis frigida, Raynaud's disease; (2) those from such anatomical abnormalities as cervical rib; (3) those from disease of the arterial wall with superimposed spasm of various degree—Buerger's disease, endarteritis, medial sclerosis, atherosclerosis; (4) conditions caused by embolism; and (5) conditions caused by injury. Sympathectomy could be of benefit only in so far as it relieved the element of the obstruction that was caused by spasm.

Muscle "Spasm" in Poliomyelitis

Mr. G. P. MITCHELL (Oxford) recalled that much attention had lately been directed to the problem of muscle "spasm" in the early stages of poliomyelitis. There were divergent views regarding its cause, nature, and importance. His own observations were that there was no true spasm except in the spinal muscles during the stage of meningeal irritation. In the limbs, limitation of passive movement was the consequence not of true spasm but of the resistance of muscles to stretch. The movements that were most restricted were those that caused traction on the main limb nerves, and if the liability to traction was increased by changes of posture —such as lateral flexion of the neck to the opposite side in cases of restricted elbow extension—the resistance to stretch was increased. Muscle resistance to stretch was simply a guarding action to prevent traction on the limb nerves. These points were demonstrated convincingly in a ciné film.

Professor J. TRUETA (Oxford) considered that the observations that had been presented provided an entirely satisfactory solution to the hitherto baffling problems of so-called muscle spasm in poliomyelitis. Mr. NORMAN CAPENER (Exeter) had found that the muscles that caused most difficulty from resistance to stretch were those, such as the gastrocnemius, that acted over two joints.

Congenital Dislocation of the Hip

Mr. E. W. SOMERVILLE (Oxford) submitted a new hypothesis based upon previously recorded facts, his own observations on cadavers of newborn infants, and on a series of 41 patients treated by operative reduction. He believed that the main factor responsible for the initial subluxation was anteversion of the femoral neck in consequence of which the femoral head exerted pressure upon the anterior part of the capsule when the limbs were extended after birth. (Pressure was minimal while the limbs remained flexed, so that dislocation before birth was unlikely.) If the capsule stretched under this pressure the femoral head was extruded from the front of the joint and lay at first antero-superiorly on the ilium. There it was so placed that the trochanteric region, by pressing upon the fibro-cartilaginous limbus of the acetabulum, turned it over into the joint, where it occupied the supero-posterior part of the cavity and formed the chief obstacle to complete reduction of the dislocation by manipulation. In every patient operated upon he had found the limbus inverted as described, and he had succeeded in producing an identical inversion of the limbus experimentally in a cadaver. His plan of treatment—which was still on trial and was not yet advocated for general use—was to remove the inverted limbus, thereby allowing complete reduction of the dislocation, and subsequently to do a rotation osteotomy of the femur to correct the anteversion and thereby prevent recurrence of the dislocation. The stage of unrestricted walking was reached within four months of the beginning of treatment. So far, the results were promising.

Mr. H. J. SEDDON (London) could not readily accept the hypothesis that the limbus played such an important part. He advised a cautious approach to open operation for congenital dislocation of the hip, recalling that a recent review of a large series of cases treated conservatively had shown that in half of them good clinical function had been retained for 30 to 50 years.

Mr. H. OSMOND-CLARKE (London) said that this was the first new and constructive contribution on the problem of congenital dislocation of the hip that he had heard for many years.

Isoniazid in Skeletal Tuberculosis

Mr. A. G. QUINLAN (Oswestry), opening a symposium, reviewed the results of the use of isoniazid in the treatment of 20 cases of skeletal tuberculosis (mainly of the spine and hip- and knee-joints). Treatment was continued for six months and no other anti-tuberculous drugs were given. His conclusions were that the drug caused marked improvement in the patient's general condition, but had no dramatic effect upon the tuberculous lesion. Dr. F. HARWOOD STEVENSON (Stanmore) recalled the laboratory and clinical observations that formed the basis for the use of isoniazid in tuberculosis.

Mr. M. C. WILKINSON (Black Notley) had studied the synovial membrane of tuberculous joints after treatment by streptomycin in some cases, and isoniazid in others. There was evidence that after streptomycin therapy healing was by fibrosis. He had hoped that isoniazid might permit healing of the synovium without fibrosis, for others had observed that effect experimentally in certain renal lesions. But a study of the synovial membrane of a shoulder-joint after two months' treatment with the drug showed evidence of persistent tubercles. Possibly two months was too short a period of treatment, but his impression was that isoniazid alone did not lead to dramatic improvement of the local lesion, and he preferred to combine antibiotic therapy with excision of the synovial membrane. Mr. Wilkinson emphasized that, despite the introduction of antibiotic drugs, a course of constitutional treatment under the best conditions was still an indispensable part of the treatment of skeletal tuberculosis. Mr. M. B. DEVAS (London) reported that ten patients with skeletal tuberculous lesions who had received antibiotic therapy with a combination of streptomycin, *para*-aminosalicylic acid, and isoniazid for six months all tolerated the drugs well, and in all cases the lesion was quiescent a year later.

Other Subjects

Other subjects discussed at the meeting included foot supports (Mr. NORMAN CAPENER, Exeter), the operative correction of fixed scoliotic curvatures (Mr. F. G. ALLAN, Birmingham, described a new method of correction), primary dislocation of the patella (Mr. J. S. ELLIS, Southampton), the treatment of dorsal adduction deformities of the fifth toe (Mr. W. H. SCRASE, Birmingham), and paralytic dislocation of the hip (Mr. G. BLUNDELL JONES, Exeter).

SIR HENRY NEWLAND, 80

Another medical man of more than national reputation, this time on the other side of the globe, is about to celebrate his eightieth birthday. Sir Henry Simpson Newland was born in Adelaide on November 24, 1873. He comes, as also does his wife, of an old South Australian family in the colony which was proclaimed under a gum tree in 1836. After he had qualified in medicine in his university he journeyed to England to take the Fellowship of the Royal College of Surgeons, studying surgery also in Paris, Prague, and Vienna, and in the United States. The year 1901 found him surgical registrar at the London Hospital, where he was a contemporary and friend of the late Sir Hugh Rigby. Returning to Australia, he built up a large practice in general surgery, and became surgeon to the Adelaide General and Children's Hospitals and lecturer in operative medicine at the university.

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During the first world war he served for a considerable time in France, where, ever in the forefront of surgical progress, he undertook a large amount of plastic surgery, then in a very early stage of development. He was with the Australian Army Medical Corps also in Egypt and at Gallipoli. In 1918, with the rank of lieutenant-colonel, he was commanding officer of the Australian section of Queen's Hospital, Sidcup, and represented his corps on the Council of Consultants at the War Office and afterwards at the Interallied Surgical Conference in Paris. He received the D.S.O. and was mentioned in dispatches.

His outstanding gifts as a surgeon have been widely recognized. Like many other medical men who have reached the front rank, he possesses something over and above acquired knowledge and technical skill—something which may perhaps be indicated, to use his own analogy in speaking of clinical acumen, as akin to the super-sense of the Australian aborigine who can see tracks in the bush unseen by the white man. His colleagues quickly found that he was not only an unusual surgeon but a very capable man of affairs, with a constructive mind. Before he was out of his 40's he was president of the South Australian Branch of the British Medical Association, which was the earliest of the Australian branches to be formed, and in 1928 he was knighted. He was a member of the Australian Federal Committee, which afterwards became the Federal Council, from 1921, and was in its chair from 1931 to the end of 1948.

Those who recall the centenary celebrations of the Association in London in 1932 will remember Sir Henry Newland as a prominent figure. In one of his centenary speeches he referred to the occasional deprecatory remark that the Association is "provincial": "If to protect the honour and interests of the profession at the farthest corners of the Empire is to be provincial we may glory in the taunt." He replied to the toast of "The Guests" on the occasion of the Association banquet at the Royal Albert Hall, which was attended by the Prince of Wales. At this meeting he was elected a vice-president of the Association.

Sir Henry Newland's last visit to this country was in 1950, when he was 76. He came in order to attend the 150th anniversary dinner of the Royal College of Surgeons, and presented a piece of plate as a gift from the Australasian College. He was the only Fellow attending on that occasion who had also been present as a Fellow at the centenary dinner fifty years earlier (he took his Fellowship in 1899). He is also an Honorary Fellow of the Royal College of Surgeons of Edinburgh and a Fellow of the American College of Surgeons and of the Royal Australasian College, of which last body he was president from 1929 to 1934. He has been a great traveller, repeatedly visiting England and journeying much in the East. After his visit three years ago he gaily set off by air homewards across the Atlantic, the North American Continent, and the Pacific.

Our latest news of him is that he is still active in medical affairs, attending meetings in different parts of the Commonwealth, and is still hale and hearty. The good wishes which go out to him on attaining the honourable estate of octogenarian will be in no way attenuated by the distances they may have to travel.

THE COLLEGE OF GENERAL PRACTITIONERS

The first annual general meeting of the new College of General Practitioners was held in the Great Hall at B.M.A. House on Saturday, November 14. The Hall was full, some four or five hundred members and associates attending from all over the British Isles and Eire.

Dr. G. F. ABERCROMBIE, Chairman of the Foundation Council, announced that a telegram had been sent to the Queen, and the following reply had been received from Sandringham: "The Queen sincerely thanks the Foundation Council and members of the new College of General Practitioners for their loyal greetings, which Her Majesty much appreciates."

The Foundation

Dr. Abercrombie, in moving the adoption of the annual report, said that on November 19, 1952, when the steering committee was dissolved, the ten general-practitioner members of that committee had to decide what was to be done next. There were two courses open to them: the first, to publish the steering committee's report and to wait and see what happened, and, the second, to found a college at once. These ten general practitioners were unanimous in their decision that, if they did nothing then, nothing would be done even after many months of argument and debate. They therefore resolved to found the College; they signed the memorandum and articles of association; their consultant colleagues of the steering committee witnessed their signatures, and the College was established. Before a year had passed, more than 2,500 men and women had joined the College—the majority in England, about 300 in Scotland, over 100 in Wales, and nearly 100 from Northern Ireland. Substantial contingents came also from Eire, Australia, South Africa, and New Zealand, and others from widely separated places all over the world. A council of the College in Scotland had been set up to deal with Scottish affairs.

Telegrams of greeting had just been received, he said, from New South Wales and from New Zealand, telling of faculties of the College founded there, and also one from Canada—from Dr. M. R. Stalker, chairman of the organizing committee of a possible College of General Practice in Canada—which said: "On behalf of the organizing committee of the College of General Practice of Canada I wish to extend to you our greetings at this your first annual meeting. The leadership of your college has been of great assistance to us, and we hope to have the Canadian college founded in 1954."

The Chairman pointed out that the College had taken no part in medical politics during the past year, and in consequence, though in contact with many organizations, was in collision with none.

The Research Programme

After giving an outline of the work of the Undergraduate Education Committee[1]—which recommended that all medical students be given an insight into general practice by general practitioners—and of the Postgraduate and Regional Organization Committee, Dr. Abercrombie described the Research Committee's programme.

Already a research register and a research advisory panel had been set up, and a research newsletter had been published. An investigation into the value of sulphonamides and antibiotics in the prevention of the complications of measles was about to begin, and a most ambitious scheme for a nation-wide survey of morbidity in general practice was being prepared in collaboration with Dr. W. P. D. Logan, chief medical statistician of the General Register Office. Study groups were forming to analyse respiratory tract diseases and to explore some of the problems of human genetics and psychosomatic disease. Obstetrics in general practice, immunization against pertussis, and the question of a nosological index were also under consideration.

In addition the research organization had in hand a scheme to observe and if possible differentiate, with the help of the Public Health Laboratory Service, the occurrence, pattern, and distribution throughout the country of minor illnesses of epidemic type—some of the pyrexias of unknown origin which were not at present receiving the attention they deserved. This project was to be called the "Epidemic Observation Scheme."

Dr. Abercrombie ended by saying that the hopes of the founders would be fulfilled only if every member and associate did something for the College. The steadily increasing burden could not be borne indefinitely on the shoulders of a devoted few. Dr. Abercrombie then announced that the Foundation Council had presented to the College a "Foundation Council Medal," to be awarded from time to time by the Council of the College for work of the highest merit in the realm of general practice, or for services of the greatest distinction to the cause of general practice.

Dr. Pickles Elected First President

In proposing Dr. William Pickles, of Aysgarth, Yorkshire, as first president of the College, Dr. J. H. HUNT, honorary secretary of the Foundation Council, said that the Foundation Council had been conscious from the beginning that it was to a great extent a self-elected body; and because of this it was hoped that the first president would be someone who had not been a member of this Council and who had not been directly connected with the foundation of the College in any way. It was common knowledge that Dr. Pickles had done a great deal for British medicine. Many practitioners before him, including William Budd and James Mackenzie, had retired from family doctoring when they became well known. But Dr. Pickles had resolutely refused to abandon his practice in spite of several temptations throughout the years, including the offer of an appointment at the Ministry of Health. Dr. Pickles would always be admired, Dr. Hunt continued, not only for his original work but also for the unshakable stand he had made throughout his life for general practice and for general practitioners. Dr. Pickles, with his outstanding academic achievements, all carried out from his country practice in a Yorkshire dale, was someone of whom British general practice might well be proud. In seconding this proposal, Dr. F. M. ROSE said that Dr. Pickles was the doyen of general practice in this country whose wisdom would be of great service to the College, and in honouring him the College would be honouring itself. Dr. William Pickles was then unanimously elected the first president of the College.

Dr. PICKLES graciously acknowledged his election, and in his reply said he felt sure that the great general practitioners of the past would have approved of the foundation of this College. He was confident that there was no one present in the Hall who did not look upon this as a solemn and historic occasion, probably one of the most momentous in the whole long history of general practice.

A Gavel from Cos

The Greek Ambassador, M. BASILE MOSTRAS, then handed the President a gift—a gavel made from the wood of an ancient plane tree from the Island of Cos, the home of Hippocrates. M. Mostras wished the new College success in its venture to maintain the high intellectual and moral standards of family physicians in this country.

In thanking the ambassador, the PRESIDENT said that this gift was a token of the friendship that exists between the two nations and was a reminder of all that Greece had done for the honour, no less than for the art and science, of medicine.

The New Council

Before the election of the first College Council, a general discussion took place on the number of members who should form this Council. In 1854 a plan for developing a College of General Practitioners failed because the committee had consisted almost entirely of those who lived in or near London. The Foundation Council had been particularly anxious that this mistake should not be made again, and that every doctor in the provinces should feel himself adequately represented, through his Regional Faculty, on the first College Council. Dr. A. BROWN, of Cambridge, proposed that the new Council should consist of 25 members, but a counter-proposal of 20 members was carried by a show of hands. It was agreed that these 20 members should be elected to the Council that afternoon. As it was desirable that each Regional Faculty should be represented on the Council by at least one member of the Faculty, the Council was authorized and requested to make from time to time, after consultation with the Board of the Faculty concerned, such additional appointments as might be necessary to secure or maintain such representation.

In the ballot, out of 37 names put forward, the 20 members of the Foundation Council who had submitted themselves for re-election were re-elected—a striking vote of confidence. The Council thus consists of four members from London, three from Scotland, one from Wales, one from Northern Ireland, and eleven from the English counties. To these will be added representatives from all those Faculties both at home and overseas which are not already adequately represented.

The constitution of the College was then reviewed and many useful suggestions were made. Dr. J. G. OLLERENSHAW, of Skipton, proposed that the annual general meeting should be held at intervals away from London. In the discussion that followed, it was pointed out that this would almost certainly mean a smaller attendance than could be expected in London; and, though it was planned to give practitioners in provincial cities every possible encouragement and help, it was felt that, for the first few years at any rate, it would be more satisfactory to hold the meeting in London. The by-laws were confirmed, with two small amendments. The feeling of the meeting was summed up by Dr. F. M. ROSE when he said: "We are here not because we think we are good practitioners but because we want to be better ones."

Votes of thanks to the Foundation Council and its officers were acclaimed, and the Chairman thanked the British Medical Association for its generosity in allowing the College to use its Hall. At a meeting of the College Council held later Dr. G. F. Abercrombie was elected Chairman, Dr. F. M. Rose Vice-Chairman, Dr. H. L. Glyn Hughes Honorary Treasurer, and Dr. J. H. Hunt Honorary Secretary.

[1] The report of this committee was published in the *British Medical Journal* on July 4, 1953, p. 36.

Nova et Vetera

JOHN HEYSHAM: A CARLISLE BICENTENARY

Get up at five in the morning, work and work till ten, and then breakfast off a quart of fresh milk and two raw eggs beaten up in hot water. Dine at two, and have supper at nine on beefsteaks and go to bed with a stiff glass of rum punch. That's what John Heysham did, and he was never ill. He lived till he was 81, and for 56 years he was one of the leading doctors of Carlisle.

Originally he came from Lancashire. He was born at Lancaster on November 22, 1753, and was educated at a little Quaker school at Yealand, in Westmorland. He served his apprenticeship as an apothecary at Burton, in the same county; and, if I may say so, training to be a doctor in those days was vastly different from what it is now. He learnt how to bleed, draw teeth, operate, and rub down his master's horse, in between times mixing medicines usually composed of aloes and rhubarb. After five years of this he went to the University of Edinburgh, then one of the leading medical schools of the world, where he graduated as a doctor of medicine when he was 24. Four years later he settled at Carlisle, living in St. Cuthbert's Lane.

He was a striking personality—so much so that he was called one of the most handsome men of the border city. Tall, well built, and energetic, he would stride about to see his patients, wearing a blue coat with silver buttons, a light-coloured waistcoat, buff trousers, and large highly polished top-boots. Long curled hair was the fashion in his youth, and Heysham's fine mane reached down to his knees. One of his close friends was the famous Dr. Paley—a great whist-player and horse-rider, as well as the author of a standard textbook on divinity. Heysham's keen interest in the natural world was drawn upon by Paley when he was composing this famous textbook.

So far nothing that I have said would mark Heysham as anything better than a most striking provincial doctor. What makes him especially notable is the work which he began within 12 months of settling in Carlisle, and which has made his name. This was the collection week by week and month by month of the records of births, marriages, diseases, and deaths of the people of Carlisle. He noted the impact upon these figures of such factors as immigration, the war against Napoleon, the weather, the price of food, the prevalence of epidemics, and many others. His accuracy and painstaking care revealed that previous tables of mortality had been seriously wrong. Dr. Price, whose Northampton tables were then the basis upon which insurance companies were calculating the premiums, estimated that the average expectation of life was 24 years; Heysham found it was 33. Price forgot to reckon with the fact that some religious denominations, like the Baptists, do not believe in infant baptisms, and so the Northampton tables had an incorrect proportion of births to christenings. Heysham's tables made no such error, and, indeed, excited the interest of Joshua Milne, the actuary of the Sun Life Assurance Company, who, with Heysham's statistics, constructed the famous Carlisle Table, which formed the basis of most of the insurance rates for many years after.

Heysham's insight into the causes of mortality led him to initiate a number of reforms in Carlisle. He discouraged the custom of tolling a bell every time a person died, or the public advertising of funerals by a town crier. He organized the establishment of a public dispensary for the city and acted as its first physician. He published an essay on gaol fever. He was the first to introduce vaccination to Carlisle, if not to the north-west, setting the practice by vaccinating his own daughter when she was a month old. He helped to establish a fever house on his own property. He promoted the paving and lighting of the streets and the construction of a canal joining Carlisle with the Solway Firth at Bowness.

But the picture which I like to cherish of him is in his role as one of Cumberland's most devoted naturalists. On his early-morning walks he would often carry a bow and arrow to collect specimens, and people would travel for miles to get his opinion on a strange bird or animal in the district. And when William Hutchinson came to write his great *History of Cumberland* (1794), it was to Heysham that he turned for information on the fauna of the county. Heysham's observations filled 53 pages of double-lined quarto in the history. And had Hutchinson written 40 years later, when Heysham was dying, he would have no doubt given another 53 pages to the record of Heysham's life.

W. H. G. ARMYTAGE.

MEMOIR OF SUDHOFF

Karl Sudhoff, the first full-time professor of the history of medicine, was born at Frankfort-on-Main one hundred years ago on November 26, 1853, and died at Leipzig on October 8, 1938, aged 85. By reason of his extraordinary industry, his tenacity of purpose, his great learning, his numerous and voluminous publications, and the many surprising literary relationships which he demonstrated, he was for many years the leading medical historian. His special achievement was to have elicited an intelligible sequence from innumerable documents of mediaeval and renaissance medicine, and thus to throw light on the sources of modern science. The most significant of his works were perhaps those on Paracelsus, on the history of mediaeval anatomy and surgery, and on epidemics. He organized the Medico-Historical Institute at Leipzig, a feature of which was an immense collection of photographs of medico-historical documents. He was a helpful and ready correspondent and a real character, so that the diminishing band of those who knew him must often recall him with a smile, for his personality was made up of obviously contradictory elements, and he was one around whom anecdotes inevitably accumulate.

In his prime he was a singularly handsome man. Well-groomed, genial, and conversational, he received younger scholars with a glint in his laughing blue eyes. Thus it took time to realize that, outside scholarship, he was a mere innocent in general outlook, that despite joviality he was comically devoid of sense of humour, and that, notwithstanding his remarkable facility in reading languages, he could be intelligible only in his native German. It was said of his learned compatriot, Immanuel Bekker, the Aristotelian, "He could be silent in no less than eight languages." Sudhoff could be unintelligibly eloquent in at least twice as many. I remember disputing with an Italian friend whether he was addressing us in English or Italian, while Sudhoff himself assured a reporter that he was speaking French, a statement fiercely denied by a French colleague. Nevertheless he was remarkably successful in interpreting a multitude of languages—on paper. In 1923, when he was 70, Professor Sigerist and I edited a volume of essays presented to him by his pupils and friends. This gave him much pleasure—and he wrote to each contributor indicating the errors that he had made. When Hitler came to power, Sudhoff, politically an infant, joined his following enthusiastically and became estranged from most of, if not from all, his foreign colleagues. He had the childlike traditional vanity of the extreme specialist. The only time that I offended him was in 1913 when my wife and I visited him on a very hot day spent at the Leipzig Exhibition. He asked me what we had most enjoyed there, and I tactlessly replied, "The swimming-bath." He was obviously hurt, but fortunately appeased when Mrs. Singer soothed him by saying, "What we really enjoyed was the stall showing your books."

At that time he was becoming dangerously obese, and in 1919, just after the first world war, he sent me a series of photographs showing him getting thinner and thinner. He explained that this was due to "the dastardly English hunger blockade." But he was a great trencherman, and I believe that the blockade saved his life. At any rate he lived for another twenty years.

All this does little justice to a man who possessed many elements of greatness. But in truth to bring those out would demand the pen and omniscience of a novelist, for whom Sudhoff would be an admirable figure. Yet those who learned the joy of scholarship from him cannot forget their debt, though they must find it hard to describe.

CHARLES SINGER.

Preparations and Appliances

ILLUMINATED CORNEAL LOUPE

Mr. H. E. HOBBS, assistant ophthalmic surgeon, the Royal Free Hospital, writes: The detection of lesions of the cornea, anterior chamber, and iris commonly presents difficulty to the student or practitioner who is unfamiliar with the technique of focal illumination with either a loupe and hand lens or a slit-lamp microscope. The illuminated corneal loupe illustrated was devised primarily to afford

undergraduate students an easier view of such lesions. It consists of a simple viewing-lens system with a magnification of 8, the focus of which coincides with that of the illuminating lens which condenses the light of a 3.5-volt torch bulb upon the object to be examined. Illuminating and viewing lenses are contained in a common mounting, and thus focal illumination of the cornea, iris, or lens is automatically achieved when the observer brings them into focus with the viewing lens. A resistance is incorporated to permit of the apparatus being used on mains current.

I have found this small device fulfil its limited purpose in undergraduate teaching, but it also makes a useful casualty inspection magnifier for the house-surgeon without ophthalmic training. Requests from colleagues for duplicates of my own model (which was made in the workshop of the Institute of Ophthalmology) have been met by its manufacture by Messrs. Stercks Martin Ltd., 56, New Cavendish Street, London, W.1, who, I understand, are able to supply it complete for the sum of 3 guineas.

The National Smoke Abatement Society has recently published two small booklets entitled *Industrial Smoke Prevention and National Fuel Policy* and *Domestic Smoke Prevention and National Fuel Policy*. The pamphlets are unabridged excerpts from the relevant paragraphs of the report of the committee on the National Policy for the Use of Fuel and Power Resources (1952, *Cmd.* 8647). They quote the recommendations relating to smoke prevention which would if adopted, in the Society's view, greatly help to reduce the "smog" in crowded and industrial areas of the country. The booklets are obtainable, price 6d. each (post free), from the National Smoke Abatement Society, Chandos House, Buckingham Gate, London, S.W.1.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Malaria in Ex-Servicemen

SIR,—In the past two years letters in both the *Lancet*[1] and *British Medical Journal*[2] have drawn the attention of general practitioners to the frequency with which men who have returned from military service abroad have been developing vivax malaria (benign tertian) in this country. The type of malaria encountered from Korea has been the non-tropical strain of *Plasmodium vivax*, in which there is a long period of six or more months intervening between primary fever and the first relapse. In the majority of instances proguanil (paludrine), 100 mg. daily, was taken regularly by British troops in Korea, and fever had been effectively suppressed while there. In many of these men, however, malarial fever has occurred in the U.K. after drug administration ceased, its onset varying from two to six months or longer according to the time when the infection had been originally acquired in Korea.

Under these circumstances, in the first relapse the temperature has often been quotidian and intermittent in type with a cold stage with shivery feelings or rigor, a hot stage, and a stage of defervescence with marked sweating. The history that the patient had served overseas should suggest the possibility of malaria and the necessity for blood examination for the identification of malaria parasites and their species. This should be done before treatment is instituted and thick and thin blood films made. By the second week, sometimes the liver, and generally the spleen, becomes palpable, haemolytic anaemia appears, and the temperature may assume tertian periodicity so characteristic of relapsing vivax malaria. By this time the clinical picture itself should suggest malaria, but I have seen several ex-Servicemen this year with fever, markedly enlarged spleens, and severe anaemia whose illness had remained undiagnosed despite the fever persisting for several weeks. From this viewpoint it is fortunate that only *P. vivax* occurs in Korea. *P. vivax* rarely kills, but in undiagnosed and neglected cases complications include rupture of the spleen, which may prove rapidly fatal, agranulocytosis, and intercurrent infections.

Outside the armed Forces and the various hospitals for tropical diseases, many patients with vivax malaria only receive treatment with schizonticidal drugs such as chloroquine ("nivaquin"), mepacrine, and quinine. While these are excellent for clinical cure of the febrile attack, they do not produce radical cure. For this purpose they must be combined with one of the 8-amino-quinoline drugs such as pamaquin or primaquine; such treatment is best carried out under medical supervision in hospital.

Falciparum malaria is common in tropical countries like Malaya and East and West Africa where British troops are serving. Fortunately proguanil, which is the common drug used for preventing or suppressing malaria in the Army, is a true causal prophylactic in falciparum malaria, destroying the early tissue forms (pre-erythrocytic forms) in the liver and preventing the appearance of the asexual parasites in the blood. Also, unlike vivax malaria, adequate treatment with schizonticidal drugs, such as chloroquine, amodiaquine, mepacrine, and quinine, produces radical cure. Furthermore, if cure has not been attained by the first course of treatment in British troops (non-immunes), recrudescences generally occur within a month. Despite these facts and the efficiency with which the Army authorities abroad are dealing with malaria, cases of fever due to *P. falciparum* are occasionally encountered in troops soon after returning to this country. Undiagnosed falciparum malaria kills rapidly in non-immunes and an early diagnosis and appropriate treatment are essential if fatalities are to be avoided.

In non-immunes, falciparum malaria is so protean in its clinical manifestations, and so difficult to diagnose clinically in the early stages, that in any obscure fever in a male of military age the practitioner should inquire whether he has recently been on service abroad. If so blood slides should be immediately examined for malaria parasites. After this, appropriate treatment can be instituted if considered advisable and arrangements made for his admission to hospital without delay.

Provided the patient can swallow and is not vomiting, chloroquine by mouth is probably the best drug to give orally in falciparum malaria; the course advised in the Army consists of six tablets (0.9 g. base) given on the first day, four tablets (0.6 g. base) on the second, and two tablets (0.3 g. base) on the third to fifth day.

In hyperinfections and in the treatment of pernicious types of malaria, whether cerebral, algid, or gastro-intestinal, quinine dihydrochloride (10 gr.) should be given intravenously, taking five to ten minutes for the injection; it can be repeated in six hours where necessary. Alternatively, mepacrine sulphonate can be given intramuscularly and repeated if necessary as with quinine.

Ex-Servicemen who have been abroad are given a copy of a "warning slip" about malaria, which is issued to men on troopships or before emplaning from a malarious area, advising them of the possibility of malaria fever developing on their return, and telling them to report to the nearest military hospital, civilian hospital, or their own doctor should they get ill. When consulting a doctor they are advised to mention the countries in which they have served overseas and any diseases—especially malaria—from which they have suffered. The dangers of malaria and the necessity for early medical attention have been emphasized.

The Hospital for Tropical Diseases (University College Hospital), London, is always prepared to investigate and admit any ex-Serviceman who has been abroad and who is suspected of malaria or other tropical disease.—I am, etc.,

N. HAMILTON FAIRLEY,
Hon. Consultant in Tropical Medicine to the Army

London, W.1

REFERENCES

1 *Lancet*, 1952, 2, 45, 288.
2 *British Medical Journal*, 1953, 2, 339.

Site for Vaccination

SIR,—I venture to suggest to Dr. J. Cantor (*Journal*, November 7, p. 1050) that a still better site for vaccination, which applies to all infants, is on the chest about 1 in. (2.5 cm.) below the right nipple. The only contraindications would be prominent chest veins or a near-by haemangioma, This site is protected from accidental injury and can easily be kept clean and dry, and the infant appears to suffer the minimum of discomfort. It is unnecessary to restrain the movement of a limb because of superficial adenitis, and in the case of females there is the additional advantage that later on the scar is completely hidden by the breast.

I have practised this method for over 15 years following a hint in one of the medical journals—I forget which—and parents, without a single exception, have been delighted with the result.—I am, etc.,

Dagenham. G. W. BENDER.

SIR,—With reference to Dr. J. Cantor's letter (*Journal*, November 7, p. 1050) concerning the site for vaccination, I believe that the sole of the foot for female infants is a well-known and quite commonly used site, the site being usually at the heel.

I used this site for a considerable number of vaccinations on female infants whilst in the Services, but gave it up for the following reasons: there were a lot of severe reactions causing large, slow-healing lesions; there were more "failed" vaccinations here than on the more usual sites; with modern techniques there is very little scarring wherever the vaccination is done.

I used the single-scratch technique on these sole vaccinations, but since giving up this site I am now using the multiple-pressure technique very successfully and with minimal scarring. If the single-scratch technique is confined to a scratch of not more than half a centimetre the resulting scar is very small too. I believe also that the immunological experts frown on vaccination on the sole and also on the thigh as being sites of poor absorption.—I am, etc.,

Swansea. G. J. VAN KLAVEREN.

SIR,—Like Dr. J. Cantor (*Journal*, November 7, p. 1050), I have been prevailed upon to vaccinate female infants on many sites. Mothers, uncertain which portions of their daughters' anatomy may be made visible by the decrees of future fashions, have a fancy for the sole of the foot. It seems unlikely that within a measurable time the human race will take to walking on its hands. After some experience I have now abandoned the sole of the foot because one baby had such an intense local reaction that oedema of the soft tissues caused pain and tearing of the epidermis. Fortunately, there was no spread either of vaccinia or of secondary infection, but I felt that the risk of ill effects following this severe reaction made the method unjustifiable.—I am, etc.,

London, W.1. ALFRED WHITE FRANKLIN.

SIR,—In reply to Dr. J. Cantor (*Journal*, November 7, p. 1050), I have been using for 10 years the sole of the foot as a site for vaccination in female children when an alternative to the arm is requested. I agree with all that Dr. Cantor has said about its desirability. There are only two things I can add to his experience. First, the skin is tougher and the vaccination not as easy as elsewhere. Secondly, I have the impression, although I may be wrong, that the reactions seem to be a little more severe than when performed elsewhere. But I have never had any trouble, and, after the arm, I think the sole of the foot is the best site for vaccination.—I am, etc.,

Tetbury. JOHN N. H. ANDREWS.

Chronic Gastric Ulcer

SIR,—I read with great interest Dr. B. F. Swynnerton and Mr. N. C. Tanner's article on "Chronic Gastric Ulcer" (*Journal*, October 17, p. 841). The critical analysis of their large number of cases should be of great value to all interested in the important problem of chronic gastric ulcer.

From my radiological studies of chronic gastric ulcer I can confirm their observation that with advancing years the location of the ulcer is usually further away from the pylorus than in the younger age groups. It may be added that ulcers in advancing years are often large, and that the so-called giant ulcers are almost exclusively seen in elderly individuals. There are good reasons for making a clear distinction between chronic gastric ulcer and duodenal ulcer, both hitherto having been considered as peptic ulcers. Swynnerton and Tanner's, and James and Pickering's[1] investigations prove that, in contrast to duodenal ulcer, super-normal secretion of acid and pepsin plays no appreciable part in the causation of gastric ulcer. Another important difference of the two conditions is the age of onset. Duodenal ulcers usually start in the third and fourth decades of life, whereas the majority of gastric ulcers occur in the middle-aged and elderly individuals, roughly in the same age groups as gastric carcinoma. Swynnerton and Tanner conclude that the association of both lesions, if at all present, could be explained by their preference for the same type of degenerative mucosa. If this were the case, we should expect a much more frequent association of gastric ulcer with carcinoma.

Bearing in mind that both diseases occur predominantly at the involutionary period of life, in which arterial degeneration plays an important part, I thought it feasible to examine chronic gastric ulcer and carcinoma of the stomach in their relationship to arteriosclerosis. In my investigations[2–4] the abdominal aorta, which usually is the site of the earliest and most extensive manifestations in general arteriosclerosis, was radiographed in 732 patients over 50 years of age. Calcified lesions of the abdominal aorta were found in 75% of 116 cases of chronic gastric ulcer, and in only 4.3% of 70 cases of carcinoma of the stomach. 190 cases of duodenal ulcer showed 34.2%, and 356 control cases 32.3%. The difference was particularly striking in the age group 50–60 (gastric ulcer 64%, gastric carcinoma 0%, and controls 17.1%).

From these findings the conclusions are drawn that the areas of degenerative mucosa in chronic gastric ulcer are most likely the result of a disturbed balance between blood

supply and demand, analogous to the pathogenesis of conditions like intermittent claudication or angina of effort. The rare occurrence of calcification of the abdominal aorta in carcinoma of the stomach is striking, and its significance for the pathogenesis of gastric cancer has to await the results of further investigations. The striking difference between chronic gastric ulcer and gastric carcinoma in their relationship to arteriosclerosis has proved, in my experience, to be a valuable aid for the radiological differential diagnosis of benign and malignant ulceration.—I am, etc.,

London, W.1. A. ELKELES.

REFERENCES

1 James, A. H., and Pickering, G. W. (1949). *Clin. Sci.*, **8**, 181.
2 *Brit. J. Radiol.*, 1949, **22**, 280.
3 *Sixth International Congress of Radiology*, 1950. London.
4 *Amer. J. Roentgenol.*, 1953. In press.

SIR,—In the *Journal* of October 17 there are two articles —"Chronic Gastric Ulcer," by Dr. B. F. Swynnerton and Mr. N. C. Tanner (p. 841), and "Hiatus Hernia and Pregnancy," by Drs. W. A. W. Dutton, and H. J. Bland (p. 864). A mechanical cause is recognized for dyspepsia of pregnancy, but not for chronic gastric ulcer. It is recorded that chronic bronchitis may complicate chronic gastric ulcer and that pulmonary tuberculosis may follow partial gastrectomy. Could not the mechanical cause, such as a linea alba hernia, cause a chronic gastric ulcer? Such a hernia could be in the posterior rectus sheath and might not then be palpable. Is a routine chest radiograph taken with each barium meal *x*-ray investigation?

In view of the association of chronic bronchitis with chronic gastric ulcer I feel that, if careful gastric histories were to be taken of men attending the pneumoconiosis medical boards, profitable research could be undertaken. Also similar histories might be taken from men under the Ministry of Pensions with leg injuries, which result in tilting of the pelvis and imbalance of the recti abdominis. The bus driver and taxi driver are believed to develop stomach ulcers from the mental strain of driving. Yet most doctors, I am sure, will agree that the mental strain only begins when they have to get out of their cars and see their patients. Perhaps these ulcers are caused, not by mental strain, but by sitting in a cramped position and allowing the abdominal muscles to waste. A cough, loss of weight, or a heavy gearbox, etc., may then cause a linea alba hernia. Do tram drivers get less dyspepsia than bus drivers?—I am, etc.,

Chasetown, Staffs. C. R. HOUGHTON.

Occipito-posterior Positions

SIR,—May I disclaim a statement attributed to me by Mr. R. G. Law (*Journal*, October 31, p. 955) in his article on "Failed Forceps"? He says, "Claye . . . was of the opinion that anterior rotation of the occiput almost invariably took place in these patients" (multiparae with occipito-posterior positions). What I wrote in the *Practitioner* article referred to was: "In multiparae, spontaneous delivery is the rule, even if the short rotation occurs." I did not comment on the *frequency* of the short or the long rotation in these patients. In fact, occipito-posterior positions in multiparae do not often attract attention unless they are delivered face to pubes, and this usually occurs without difficulty.—I am, etc.,

Leeds. ANDREW M. CLAYE.

SIR,—In his recent article on failed forceps deliveries Dr. R. G. Law (*Journal*, October 31, p. 955) gives two main malpositions of the foetal head as "occipito-transverse and occipito-posterior positions." In using the term "occipito-transverse," which has slipped into the obstetrician's vocabulary in recent years, Dr. Law is probably unaware of the pain it causes to pedants and the confusion it may cause to students. The *foetus* may lie transversely, the foetal *head* may be arrested transversely, but the *occiput* can only be described as facing anteriorly, posteriorly, or *laterally*. Or perhaps Dr. Law and others look upon this terminological exactitude as being, in brief, a L.O.T. of R.O.T.—I am, etc.,

Walton-on-Thames. R. M. EMRYS-ROBERTS.

Use of Obstetric Forceps

SIR,—Professor T. N. A. Jeffcoate (*Journal*, October 31, p. 951), in his excellent paper on the use of obstetric forceps, advocates trial of forceps, but neither in his paper nor in your editorial comment is there any reference to a danger of the method of which I have had unhappy experience recently.

In a case of trial labour, where forceps were applied tentatively to a head in mid-cavity and where it was decided that pelvic contraction was such that to proceed with forceps delivery would be dangerous, a caesarean section was carried out and the child delivered 45 minutes after the original induction of anaesthesia. It proved impossible to resuscitate the child, and this was attributed to respiratory depression due to the prolonged inhalation anaesthesia which had been used. At necropsy there was no evidence of intracranial injury, but a complete atelectasis was found in both lungs.

Local analgesia is unsuitable for the higher forceps operations, and it seems, therefore, that this is an inescapable risk of the method of trial of forceps. The susceptibility of infants to anaesthesia, of course, varies enormously, and in most cases the prolonged anaesthesia will give rise to no difficulty, but there will always remain a proportion of cases in which the child will be lost because of this factor. In consequence of this a very careful assessment of the prospects of forceps delivery is necessary before trial of forceps is undertaken, and it is not a method to be employed indiscriminately. The safety of the operation would be increased if it were carried out in an operating theatre with all preparations already made for caesarean section, in the same way as examination under anaesthesia in cases suspected of placenta praevia.—I am, etc.,

Worcester. J. A. CHALMERS.

SIR,—May I say how much I enjoyed reading Professor T. N. A. Jeffcoate's article on "The Place of Forceps in Present-day Obstetrics" (*Journal*, October 31, p. 951)? It is encouraging to have such eminent support for matters which one has taught students with diffidence. I am referring in particular to two points made by Professor Jeffcoate.

The first is that forceps delivery should not be deferred because of second-stage inertia. For too long now it has been taught that the absence of contractions contraindicates forceps delivery. Provided that the danger of post-partum loss is remembered and that block analgesia is used wherever possible, coupled with the use of ergometrine, the dangers of deferring delivery are greater than those of completing the labour by forceps.

Secondly, it is high time that we were less afraid of referring to "trial of forceps," although we must, of course, realize that the occasions which justify such a procedure are few. I would like to add one suggestion to Professor Jeffcoate's remarks. When difficulty in forceps delivery is anticipated, trial of forceps should be carried out in the theatre with caesarean section instruments laid out and the sister scrubbed up, just as one would have for examining a patient suspected of placenta praevia. There would then be still less incentive to proceed to vaginal delivery at all costs.—I am, etc.,

Bristol. T. F. REDMAN.

SIR,—The most excellent article "The Place of Forceps in Present-day Obstetrics" by Professor T. N. A. Jeffcoate (*Journal*, October 31, p. 951) can hardly be allowed to pass without comment. Under the heading of causes of decreased risks, the author includes "the discarding of all forms of axis-traction instrument." Only a few years ago I was taught obstetrics at a London hospital, where I believe the teaching was of a modern and fairly uncontroversial kind. Here I was taught always to apply the axis-traction rods, and I still carry this teaching out in general practice except when applying the Wrigley forceps, which have their own indications for application.

If axis traction were applied purely for obtaining a better purchase for the hands of the operator, I would agree entirely with Professor Jeffcoate, but I cannot believe that this is ever done by anyone qualified to apply them. Rather

would I suggest that the less experienced the operator the more important is it for him to apply with axis traction, as it is his surest and safest method of knowing for certain that his line of traction is correct all the time during the descent of the head. I have never been impressed with the effectiveness of Pajot's manœuvre.—I am, etc.,

Princes Risborough. M. W. FORDHAM.

Standardization of Syringes

SIR,—I keep my 2 ml. syringe in a modified adaptation of the killing bottle—an elegant electro-plated cylinder charged with antiseptic, or even bactericidal juice. But sometimes the syringe gets broken, and then the hunt is on to find a workable replacement.

The first one I get is a bit too thin at the shoulders, and straightway drops to the bottom of the container, turning the rapier point of my No. 15 g.p. (general *purposes*) needle into a sadistic hook fit only for the treatment of temporary patients. My next purchase is just a fraction too thick at its lower metal end and will not go in at all. This thickening I proceed to reduce on my electric grindstone, but the heat generated thereby is great, and all of a sudden I am confronted with a transverse fracture of the glass barrel at the junction of its middle and lower thirds. All goes well with my third syringe till I attempt to screw on the treacle-tight head of the container, when, blow me ! the operation is made impossible by the piston rod, which I discover to be exactly one-eighth of an inch too long. I resect a small portion of this rod, but fail miserably to complete the operation by an end-to-end anastomosis.

We live in an epoch of "advance." We split the atom, measure the circumference of Orion's belt, spend four hundred millions on "health," say ml. instead of c.c., so why the heck cannot we achieve a standard-size Record syringe ?—I am, etc.,

Buxted, Sussex. W. R. E. HARRISON.

Lead in Lollies

SIR,—Your correspondent Dr: R. C. Hoather (*Journal*, October 31, p. 993) states that the Food Standards Committee recommended for beverages "ready to drink"—other than beer, cider, or apple juice—a maximum lead content of 0.2 p.p.m.

Dr. Charles Hill, Parliamentary Secretary to the Ministry of Food, is reported (*Hansard*, October 22) as stating that the Food Standards Committee was of the opinion that the maximum content of lead in food generally should be two parts per million. Is this distinction of a decimal place dependent in the lollies controversy on whether we regard the ice lolly as a solid or a liquid ? The subject becomes even more confusing when yet another decimal place decides the generally accepted maximum permitted quantity of lead in drinking water as 0.02 p.p.m.

I, and I am sure many others, would welcome some "clarification" of this subject, with an especial plea that in the future setting of standards of such importance in food and water the decimalization of numbers such as 1, 2, and 5 should be avoided.—I am, etc.,

Beckenham, Kent. L. R. L. EDWARDS.

"Smog"

SIR,—May I, as chairman of the local medical committee for the County of London, thank you for reporting in full, under "Medical News" (*Journal*, November 7, p. 1055), the resolution it passed on October 27 concerning the fog disaster of December, 1952 ?

It was interesting to read in your issue of the same date the letters of Drs. W. McNaughtan and L. Crawford (p. 1048). The first says, apropos the wearing of gauze masks during a fog, that "it seems likely that a loose plug of cotton-wool in each nostril would act fairly efficiently provided there is no mouth breathing," and goes on to state that "the value of this method can be tested by anyone using it in their coal cellars for a time." The second letter states that a mask of the usual pattern used in operating theatres was worn without success during the operation of shifting coal from the entrance to the far end of a coal shed. May I assure both these writers that London fog is of a different nature altogether from the unburnt coal-dust encountered in a coal cellar or shed ?

Years ago I tried the little bit of cotton-wool loosely inserted into the nostrils, but gave it up because of the heat and secretion resulting. In fog a surgeon's mask works amazingly well. I have used it in several fogs and during the more or less continuous three- to four-day fog of last December in my part of London, when car driving was wholly impracticable. I walked each day approximately six to eight miles wearing a surgeon's mask and suffered none of the ill results that the theorist in the Ministry of Health forecast. The mask was changed each time I got back to either home or surgery for one hanging out to dry. I washed out the masks myself; practically all the soot was in the outer layers of the gauze. I found that the dampness of my breath condensing on the inner aspect of the mask increased the cover of the mask. In consequence I could cut down the number of masks in use, as one still damp from the wash was all the more effective.

My ambulant bronchial, asthmatic, and heart patients did well if they followed this advice: Go home—stay home; shut all doors and windows tightly; sit in bed or chair with a small coal fire burning (not smouldering). At the Centenary Annual Meeting of the B.M.A. in 1932 there was a demonstration which showed how the red rays of an electric or gas fire caused constriction of the nostrils and more difficult breathing. Those chronically ill at home who are willing to try the experiment can also wear a gauze mask if the fog still penetrates in spite of shut doors and windows. It is, however, a well-known fact that the fog indoors is never so thick as that outside. This, I believe, adds importance to the first part of my slogan (Go home—stay home) for those who suffer from respiratory embarrassment.

To protect my patients, and somewhat to their surprise, I have worn a mask in the surgery when I have had a cold. One might hope that the Ministry of Health, knowing the relative amount of sickness and loss of manpower caused by acute colds and their infectious nature, might gain considerable kudos if, while the interest in fog masks lasts, it were to suggest that the cold-suffering public might well put on their masks and reduce passing their colds on to colleagues at work.

In conclusion, neither I nor any of my colleagues have ever claimed that a suitable mask was anything other than a partial barrier. The prevention of "smog" lies with Parliament and the several Ministries concerned.—I am, etc.,

London, W.10. HUGH H. D. SUTHERLAND.

SIR,—Dr. L. Crawford (*Journal*, November 7, p. 1048) expresses doubt about the efficiency of a gauze mask, such as is worn by surgeons, in keeping out solid particles of "smog," because of a wide gap between face and mask along its upper border. I would suggest that in this case the mask is being worn incorrectly and that, if worn by a surgeon in such a manner, would entirely defeat the purpose for which it was meant. If the mask is worn well up under the eyes, the elevation caused by the bridge of the nose is negligible and the fullness of the cheeks below obliterates any gap.—I am, etc.,

Chigwell, Essex. CONSTANCE P. F. THOMAS.

A Chemically Treated Mask

SIR,—The frame of the mask is made of 1/16 in. (0.16 cm.) wire shaped to the contour of nose and face. It extends from the middle of the nose and fits along the hollow between the chin and the lower lip. Its length is about 3½ in. (8.7 cm.), and breadth 2½ in. (6 cm.). On this 12 layers of gauze are stitched round the wire. The gauze is trimmed about ½ in. (1.25 cm.) from the stitches, thus leaving a fluffy edge. The gauze is previously soaked in a saturated solution of bicarbonate of soda, made with a little alcohol, tragacanth, and water, then dried, or the inner layers of gauze are rolled in bicarbonate powder using untreated gauze for the two outer layers. This close-fitting mask with its fluffy border renders the passage of "smog" particles impossible. Dr. L. Crawford (*Journal*, November 7, p. 1048) could shovel coal for a day with such a mask without finding any particles

on the inner surface. Plugs of cotton-wool in the nostrils would, of course, be useless, owing to the nasal secretions damping the wool. The impregnation with $NaHCO_3$ neutralizes sulphur dioxide, hydrogen sulphide, or any other acid gases which may be present in the air. Even if these acid gases are dissolved in floating droplets the mask will trap them and render them harmless. I have tried this mask using cigarette ash and other finely divided particles. For acid fumes I have tried it with acetic acid vapour, using spots of bromthymol blue as an indicator ($pH = 6.0–7.6$). The wire frame was made for me by a dentist friend—Mr. Thomas Howe—from a plaster cast; and it can of course be made to fit any adult face by appropriate squeezing or stretching. It costs about 6d., and can be carried in the pocket. Gauze layers can be renewed when necessary. Breathing is easy and speaking is unaffected.—I am, etc.,

Greenford, Middlesex. ROBERT FLEMING.

Hydrocortone and Soft-tissue Lesions

SIR,—In the communication on the above subject by Dr. J. Cyriax and Dr. O. Troisier (*Journal*, October 31, p. 966), allusion is made to a diversity of topics, some of which invite further comment.

The communication contains the affirmation: "*Capsular Pattern.*—If the entire fibrous cuff about any joint is found contracted arthritis is present." The description of a contracted fibrous cuff about a joint, though somewhat metaphorical, indicates that the pathological process is of a periarticular nature rather than an arthritis. This is well seen in the frequent condition usually designated "periarticular fibrositis of the shoulder," which apparently corresponds to the condition named "freezing arthritis of the shoulder" by Dr. Cyriax. Here, although the painful limitation of movement may be severe, there is no effusion or swelling of the shoulder-joint, and the skiagram is normal, the morbid changes being strictly periarticular.

There are extant two records of necropsies of this condition, performed upon subjects who had died of intercurrent events while undergoing treatment for the shoulder. In both of them the intermuscular planes and the tendons were observed to be dulled and roughened, with the formation of minute adhesions; the shoulder-joint itself was found to be quite normal. It would thus appear that the cases regarded by Dr. Cyriax as arthritis of the shoulder, and treated by injections into the joint and otherwise, were actually suffering from a periarticular process.

In cases of this nature, as in other comparable lesions of the soft parts, the essential clinical feature is the tendency to spontaneous recovery. However painful and protracted the symptoms, the restoration of function is ultimately complete. It is thus difficult to compare the value of different forms of treatment. The alleviation of pain is a definite benefit, and so are these measures which maintain hopefulness and encourage the voluntary use of the affected member.—I am, etc.,

Sheffield. R. G. ABERCROMBIE.

Lumbar Puncture

SIR,—In the detailed description of lumbar puncture by Dr. William Gooddy (*Journal*, November 7, p. 1040) one important practical detail is omitted. The position of the operator is just as important as that of the patient. To ensure a certain, painless, and effective puncture, the needle should be held between the forefinger and thumb, by the butt; the shaft must never be touched. The operator must then get his eye in the line of flight, as in playing darts. This is best achieved by kneeling down beside the bed. The operator can then visualize exactly the direction of the point in all planes, and be certain of hitting the theca in the central plane.

When spinal anaesthesia was in vogue some years ago an experience of some hundreds of personal injections convinced me and many generations of residents that this was the only fool-proof method. How often has one seen inexperienced residents, and even trained anaesthetists, wasting time, and causing needless anxiety and suffering to the patient, by standing with their line of vision well away from the needle, and therefore not having the least idea of the position of the point. Incidentally, it is debatable whether a local analgesic is really necessary for the expert operator.—I am, etc.,

Worcester. NORMAN DUGGAN.

Backward Readers

SIR,—The Army survey of illiteracy among recruits, quoted in your leading article under the above heading (*Journal*, August 22, p. 433), adds support to the growing body of evidence that there is, in normal populations, a "hard core" of illiterates of the order of 1%. The same proportion was arrived at in the Ministry of Education survey, which you also mentioned; Hallgren[1] found a similar figure in Sweden, and, in his extensive review of the literature, noted that American estimates were largely in agreement in placing the incidence of illiteracy at about 1% of the population.

The consistency of this figure, in countries which have made every effort to achieve universal literacy, suggests that some more concrete disability may form the basis of the "hard core," rather than influences such as standards of education, domestic environment, or emotional maladjustment. It seems more likely that the majority of these stubborn illiterates are cases of specific dyslexia, for which, since Hinshelwood's[2] description and analysis (though under a different name), a physical basis has been argued. The physical nature of dyslexia was further emphasized by Orton,[3] in his theory of interference of the minor hemisphere in the reading process and his demonstration of concomitant disabilities in writing; while Hallgren has traced the inheritance of this disability and proposed a genetic basis for its transmission.

The neurophysiological basis of specific dyslexia is still unsolved, but its reality as a disability is none the less apparent to those who deal with handicapped children. The syndrome is remarkably consistent, and one of its features is the frequently poor response to treatment and remedial training. Not only is the response poor in the matter of learning to read, but the constant emphasis on his disability, the bandying about of phrases like "word blindness," and even the threat of certification as mentally deficient may produce the most unhappy patient.

There is surely a case for diminishing the severity of the stigma implied by "illiteracy," and for assisting the dyslexic to make the best use of his other abilities.—I am, etc.,

Kampala, Uganda. JOHN MCFIE.

REFERENCES

1 *Acta psychiat. neurol. scand.*, 1950, Suppl. 65.
2 *Congenital Word Blindness*, 1917. London.
3 *Reading, Writing, and Speech Problems in Children*, 1937. London.

The Human Foot

SIR,—I should like to add a contribution to the correspondence on children's footwear. Long experience in child welfare clinics has taught me never to allow an infant or toddler to leave the consulting room without personally removing shoes and socks and examining the feet. Invariably, if a child is wearing ankle-strap shoes or laced shoes too loosely tied, or shoes too large in the heel for the particular child although adequate in length, or if button or buckle has not been altered to ensure snug heel fitting, I find the luckless infant has crushed toes, with corns in very many cases, even at a very tender age. For the foot slips forward in the shoe and toes curl up and are crushed against the front leather if not held back by secure fastening.

The very young child with the long narrow foot, or one with a small heel and broad forefoot (I and my son suffer from the latter and my daughter from the former) are not catered for in cheaper footwear in the smaller sizes of toddlers' shoes. And the fat child with a high instep has a very difficult time indeed. There are still too many relatives who send fancy slippers as presents to grandchildren or nieces, and mothers who buy the "next size" without taking the toddlers for fitting. And recently I have

discovered poor crushed little toes on removing the modern miniature woolly-lined boot. The flat-footed, knock-kneed child wearing soft crêpe-soled shoes or Wellington boots improves enormously if provided with a properly fitted built-up shoe, or, when price is a consideration, a locally made clog.

May I make the following recommendations: Babies in prams should never wear shoes, and shoes need not be worn till the toddler is ready to walk out-of-doors; no short or tight fitted socks should be worn; manufacturers of cheaper shoes should emulate those of more expensive types and make several fittings for same length; only expert fitters should fit children's shoes, and all shoe-selling assistants should have a course of training in the infinite variety of children's feet; ankle-strap shoes and woolly-lined boots for children should be discouraged; all mothers and nurses should be taught to discard tight socks and to tie shoe laces securely.—I am, etc.,

Manchester. MABEL LINDSEY.

SIR,—Dr. G. G. Sherriff's comments (*Journal*, November 7, p. 1048) on my account of foot defects in children (*Journal*, October 3, p. 749) raises two important points.

First, on the question of the shoe as a deforming agent, far too many shoes, as Dr. Sherriff points out, are so shaped that they constrict the toes of their wearers. Although I did draw attention to two particularly detrimental types, the "pointed toe" and the "casual" shoes, I found as much harm being done by shoes which were intrinsically well shaped, but which were either still being worn when outgrown or which were an incorrect fitting for the particular feet they covered. While well-shaped shoes are so expensive there is a grave danger that parents enlightened enough to buy them will be tempted to make them last just a little longer than they should, and the majority of parents will be unable to pay the extra to ensure that their child wears a shoe fitted for width as well as for length.

However, I cannot agree entirely with Dr. Sherriff's plea for a completely straight inner border. In many feet, from the age of 10 upwards, there is considerably greater width of bone at the level of the first metatarso-phalangeal joint than at the level of the first interphalangeal joint, even when the great toe is quite straight. Hence, unless the toe is actually in a varus position, a slightly convex inner border gives a better fit. There should not be more than 10 degrees inward deviation. The old rule that half the great toe should lie outside a line drawn along the inner border of the heel is still true.

As regards Dr. Sherriff's second point, while criteria may vary, I feel it is of utmost importance to detect and prevent early functional inefficiency at this stage, rather than to aim at seeking out anatomical imperfections.—I am, etc.,

London, N.21. DORIS A. CRAIGMILE.

Effects of Atropine Mucate

SIR,—The interesting article by Dr. William W. Mushin *et al.* on the effects of atropine (*Journal*, September 19, p. 652) stimulated me to look up some old unpublished records of mine.

After reading Drs. W. A. Bain and J. L. Broadbent's letter (*Journal*, June 25, 1949, p. 1137) on the initial bradycardia following the subcutaneous injection of atropine I then endeavoured to discover if this also followed the intravenous administration of the drug. Accordingly atropine sulphate 1/100 gr. (0.65 mg.) was injected slowly into some 30 unselected conscious and unpremedicated patients whose ages ranged from 3 to 64 years. Their pulse rates were checked immediately before the injection and again two minutes afterwards. In 23 of these patients there was an initial increase in pulse rate, but in 6 there was no change, and in 1, a male aged 58, there was an initial slowing from 64 to 56 per minute.

When employing vagolytic and ganglionic blocking agents in association with nitrous oxide and pethidine anaesthesia during the past 3½ years it has been my practice when necessary to inject 2.5 mg. of neostigmine and 0.65 mg. of atropine together very slowly towards the end of the operation, and I have not observed any undue bradycardia to follow this. On the other hand, in vagotonic subjects such as those with jaundice, asthma, peptic ulceration, obesity, sinus bradycardia, and those who have been digitalized, and particularly when cyclopropane has been the anaesthetic agent used, the preliminary injection of 1/50 gr. (1.2 mg.) of atropine should be regarded as essential and precede the injection of 2.5 mg. of neostigmine by some 10 minutes, and as a final precaution the patient should be kept under observation for a further 10 minutes after the latter injection.—I am, etc.,

Hull. W. N. ROLLASON.

Transfusion in the Field

SIR,—The following account of the use of a primitive method of blood transfusion in the field may be of interest to some of your readers. The writers were travelling in the northern part of Karamoja—the northern province of Uganda—when they came across one of the local inhabitants who had a wound from a spear which had transfixed the right chest at about the third intercostal space. The wound had been inflicted at about 8 a.m. He was seen at about 4 p.m. He was being taken to hospital in a truck by two European missionaries. His wound had been dressed by Mr. Deschler, an anthropologist, whose camp was near by. When examined, he was cold, his respiration was distressed, and he had orthopnoea. His pulse was 160 and of poor volume, the right side of his chest was dull, and his apex beat displaced nearly to the left axilla. It seemed doubtful whether, without further treatment, he would survive the 90-mile journey over rough roads to hospital at Moroto.

We took him to Mr. Deschler's camp a few miles away. He was given about 1½ pints (0.85 l.) of hot sweet tea, ½ gr. (32 mg.) of morphine, and 300,000 units of procaine benzylpenicillin ("distaquaine"). We had with us two fairly wide bore needles. We borrowed a piece of rubber tubing (the normal function of which was to siphon petrol into the tank of Mr. Deschler's car). A needle was placed in either end of the tubing, and the apparatus boiled in saline made by adding a teaspoonful of salt to a pint of water. One needle was inserted into the median basilic vein of the donor (we are both group O) and the other into that of the patient, while the donor maintained a pumping action by compressing his upper arm and clenching and relaxing his fist. This was continued for 10 minutes, when it was obvious that the blood had clotted in the needles. The procedure took place in the back of the truck.

The final touch was added when the truck resumed its journey, the back containing the patient, his mother, one of his wives, the assailant, the spear, and an askari (policeman) with his rifle and ammunition. We heard subsequently that the patient made an uninterrupted recovery and was out of hospital in 10 days. We should add that this was not an incident arising from the recent enthusiasm for cattle raiding in the vicinity. The wounded man and his assailant had merely had a family quarrel about a cow. One of us was carrying a fairly complete medical kit, as he was on holiday with his wife and two small children, and the district is somewhat remote.—We are, etc.,

ERIC HOLMES.
Kampala, Uganda. MARGARET THOMPSON.

Royal Medical Benevolent Fund Christmas Gifts

SIR,—I venture to remind your readers of Lord Webb-Johnson's Christmas Gifts Appeal (*Journal*, October 3, p. 777).

The distribution of gifts is made well in advance of Christmas Day, and I earnestly hope that those who have not yet responded to the appeal will send their contributions as soon as possible to the Secretary, Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S.W.15, marked "Christmas Gifts."—I am, etc.,

London, S.W.15. FRANK JULER,
Honorary Treasurer.

Obituary

T. G. STEVENS, M.D., F.R.C.S., F.R.C.O.G. M.R.C.P.

Many old students of Guy's Hospital and St. Mary's Hospital will be sorry to learn of the death of Mr. T. G. Stevens, which occurred at Bournemouth on November 10. He was 84 years of age. Mr. Stevens was consulting obstetrician to St. Mary's Hospital and to Queen Charlotte's Maternity Hospital and consulting surgeon to the Hospital for Women, Soho Square. For a time he acted as gynaecologist to the Mildmay Mission Hospital.

Born on March 25, 1869, Thomas George Stevens was the son of Dr. G. J. B. Stevens, and was educated at St. Paul's School, receiving his medical training at Guy's Hospital Medical School. He qualified M.R.C.S., L.R.C.P. in 1890 at the early age of 21, taking the London degrees of M.B., B.S. in the same year, with honours in medicine. After qualification he filled the posts of house-surgeon and resident obstetric officer at Guy's Hospital and acted as resident medical officer at Queen Charlotte's Hospital and the Evelina Hospital for Children. He proceeded to the M.D. in 1892, obtained the diploma of F.R.C.S. in 1895, and was admitted M.R.C.P. in the following year.

During the period of waiting for a staff appointment Stevens filled the post of demonstrator of biology at Guy's Hospital Medical School, and for a time examined in biology for the Conjoint Board. In 1899 he was elected assistant surgeon to the Hospital for Women, and in 1902 he became obstetric tutor at St. Mary's Hospital Medical School. In 1908 he was appointed to the staff of Queen Charlotte's Hospital, and in 1912, on the retirement of the late Dr. C. M. Handfield-Jones, was elected assistant obstetric surgeon to St. Mary's Hospital. Two years later, on the premature retirement of the late Dr. W. J. Gow, he was promoted to the senior staff. At the beginning of the first world war Stevens was for a time in sole charge of the obstetric and gynaecological department at St. Mary's. From 1914 to 1934 he was at the height of his career, working hard at his hospital and in his extensive private practice. He was the author of *The Diseases of Women* (1912), and he contributed to the well-known textbook by the "ten teachers." He also wrote many articles dealing with the technicalities of his specialty. For some years he acted as examiner in obstetrics and gynaecology for the Conjoint Board and for London University. When the British Medical Association held its Annual Meeting at Aberdeen in 1914 he served as a vice-president of the Section of Obstetrics and Gynaecology, and he held similar office at the Winnipeg Meeting in 1930. A Foundation Fellow of the British (now Royal) College of Obstetricians and Gynaecologists, he was a member of the council from 1929 to 1935, and also served on the examination committee and the fellowship selection committee of the College. He retired in 1934 and went to live at Bournemouth.

Stevens was expert in his professional work, being a skilful operator and an excellent and popular teacher. A colleague recalls an occasion when he successfully performed an operation for the removal of a gigantic fibroid so big and heavy that it was necessary to rig up a pulley and tackle to support the tumour during its removal. Stevens was short in stature, and he wore a small, pointed beard. His sense of humour was well developed, and his wit could on occasion be rather caustic, but his eyes often had a merry twinkle in them. A clever artist, he was particularly good at painting interiors. He enjoyed golf and fishing. He was a keen freemason and filled the chair of the Sancta Maria Lodge in 1917.

Mr. Stevens lost his wife a year ago. His son, Mr. T. Russell Stevens, is a surgeon on the staff of the Dorchester County Hospital, and to him we tender our sympathy.

A. M. FLEMING-BERNARD, C.M.G., C.B.E. M.B., F.R.C.S.Ed., D.P.H.

Dr. A. M. Fleming-Bernard, medical director of Southern Rhodesia from 1898 to 1931, died at Edinburgh on November 6 at the age of 82.

Andrew Milroy Fleming—he changed his name to Fleming-Bernard in 1946—was born at Edinburgh on January 28, 1871, the son of the Rev. John Fleming. After receiving his early education at Edinburgh Academy and Durham School, he entered Edinburgh University as a medical student, graduating M.B., C.M. in 1893. He then held the appointment of assistant physician at the late Sir Robert Philip's Victoria Dispensary for Consumption and Diseases of the Chest at Edinburgh until 1894, when, for family reasons, he went to South Africa, becoming junior surgeon at the hospital at Kimberley at the time of the diamond boom. He became a great friend of Charles Coghlan—later Sir Charles Coghlan, the first Premier of Southern Rhodesia—and through him was introduced to Dr. (later Sir Leander) Starr Jameson, who was looking for medical officers for Mashonaland, then newly occupied by white people. Fleming thereupon moved to Salisbury, Southern Rhodesia, at the end of 1894, and for some weeks was the only medical officer in an area of some thousands of square miles. With no modern aids, in the most primitive surroundings, he was called upon to deal with every type of injury and illness. In 1896, on return from furlough—during which he had married Miss Philadelphia A. Fisher—he found the Mashona rebellion in full swing, and the last part of the journey, from Beira to Salisbury, had to be made on foot and in dangerous circumstances, since murders of white settlers were frequent. In Salisbury his services were of immediate use in dealing with the wounded and injured, and he also acted as medical officer to the laager into which the women and children had been taken for safety. For his services he was appointed C.M.G. in 1898, and at the age of 26 became one of the youngest recipients of that honour.

Fleming was appointed medical director of Southern Rhodesia in 1898, and from that date really began his lifework of building up a health service for the growing colony. Starting with virtually nothing and himself responsible for most of the major surgery as well as the administration, he slowly but surely collected a faithful band of medical men ready to devote themselves to the needs of the settlers and of the indigenous population alike. In 1903 he took the F.R.C.S.Ed. and the Cambridge D.P.H. diplomas, signifying the dual role he was called upon to play in Southern Rhodesia. He designed and superintended the building of hospitals and training-schools for nurses, and he drafted health legislation, which, as a member of the Legislative Council, he helped to pass. During the first world war

Fleming obtained leave to volunteer, and in 1915–16 saw service in Poland and Russia, where much work was necessary to combat typhus and dysentery epidemics.

In 1923, with the advent of responsible government in Southern Rhodesia, Fleming took the opportunity entirely to remodel the medical and nursing services of the colony, as well as to produce entirely new health legislation. On these foundations the whole of the colony's present health services have been built, and from them they will be extended in the future. For this work he was appointed C.B.E. in 1924. On his retirement in 1931, after 37 years of tireless and devoted service, Fleming had the satisfaction of knowing that he had established ten major general hospitals, a mental hospital, and a leprosarium, as well as laboratory services, a medical service of over twenty officers, and two training-schools for nurses—no mean achievement with the meagre funds at his disposal.

For a few years after he had retired from the post of medical director of Southern Rhodesia Fleming continued to practise as an estate medical officer, but in 1946, on inheriting the estate of Dunsinnan, near Perth, he returned to Scotland and assumed the name of Fleming-Bernard. He spent the rest of his days on his estate, although he made several flying visits to the Rhodesia he loved and for which he had given so much of his life. Those who were privileged to work for and with him retain as an abiding memory his well-directed energy, his high ideals, and his devotion to duty. If these ideals at times bore hardly on his subordinates, it is proper to remember that he never asked more of them than he himself was constantly giving. He was ever an inspiration to his junior staff. His monument can be seen in every Southern Rhodesian centre, and his memory will ever be honoured in the colony.—R. M. M.

Mr. ARTHUR GREENE, who died at Cromer on October 20 at the age of 77, was a member of an old Irish family and the third son of Mr. Thomas Greene, at one time High Sheriff of County Kildare. Born at Dublin on January 3, 1876, Arthur Greene was educated at the High School there and at Trinity College and the Royal College of Surgeons in Ireland, graduating M.B., B.Ch. in 1898; in the same year he proceeded to the M.D., and took the L.M. diploma at the Rotunda. In 1908 he was admitted to the Fellowship of the Royal College of Surgeons in Ireland. After graduation he held appointments as house-surgeon and registrar at the Royal Eye Hospital, London, and clinical assistant at the Royal Westminster and Moorfields Eye Hospitals before settling in practice at Norwich in 1903. He was the first specialist to be appointed to the staff of the Norfolk and Norwich Eye Infirmary as a whole-time ophthalmic surgeon. It was very largely due to his efforts that the old Eye Infirmary in Pottergate was moved in 1912 to a more suitable site opposite the Norfolk and Norwich Hospital, with which it was later amalgamated. Mr. Greene was on the staff of the eye infirmary for over 37 years. During the 1914–18 war he saw service with the R.A.M.C. in France and was for some time ophthalmic surgeon to the 5th Army. A member of the Ophthalmological Society of the United Kingdom since 1903, he attended its annual meetings regularly for a great many years. He had served as a member of the council of the Oxford Ophthalmological Congress, and was a past president of the Norwich Medico-Chirurgical Society. He was one of the founder members of Toc H in Norwich, and he rarely missed any meetings of the Norfolk and Norwich Archaeological Society, in which he took a lively interest. He leaves a widow and a son, who is chaplain of Kelling Sanatorium, Holt.—G. M.

The death occurred on October 10, while he was on holiday, of Dr. G. F. MITCHELL, of Rugby, at the age of 62. George Fowler Mitchell was born at Aberdeen on July 16, 1891, and was a medical student there, graduating M.B., Ch.B. in 1917. As a student he won the Fife Jamieson gold medal in anatomy. After graduation he was a house-surgeon at Aberdeen Royal Infirmary before entering the R.A.M.C. for service in the war of 1914–18. For a time he was pathologist to the 40th British General Hospital in Mesopotamia: while there he collected statistics on the treatment of local leishmaniasis, and, after putting his findings into writing, submitted them as a thesis for his M.D., which he obtained with a commendation in 1921. After demobilization he held various appointments at the Hospital for Sick Children, Great Ormond Street, until 1921, when he settled in practice at Rugby, where he became also a member of the surgical staff of the Hospital of St. Cross, and, later, the senior surgeon of the hospital. Only an occasional contributor to the medical literature, Dr. Mitchell was particularly pleased when, in 1933, his article entitled "Total Avulsion of the Scalp—a New Method of Restoration" (which was published originally in this *Journal*) was translated into Italian. Dr. Mitchell was appointed a serving brother of the Order of St. John of Jerusalem in 1945, and he was a past president of the Rugby Medical Society, having been in earlier days its honorary secretary. He was also a keen Rotarian. For the past two years friends tried to persuade him to do less and to take the rest he deserved, but he wanted to go on. At last he began to realize that he was overworking himself and he went away for a restful holiday, after dealing with a number of exhausting emergency cases, but it was too late. Symptoms of heart trouble appeared almost on his arrival at Tenby, and despite every care he died. Dr. Mitchell loved the simple things in life; he loved the Hospital of St. Cross; but above all he loved his family, and he never tired of telling of some achievement of his wife, his son, or his daughter, all of whom survive him. A simple memorial service in the chapel of the hospital was attended by his personal friends and by those with whom he worked.—R. E. S.

The death occurred on October 23 of Dr. FRANK GEOFFREY HOLMAN, of Stanmore, Middlesex, at the age of 44. He was a medical student at Guy's Hospital, and after qualifying he held an appointment as house-physician at the Hospital of St. John and St. Elizabeth, and then settled in practice in North-west London. For some years he was a member of the executive committee of the Hampstead Division of the British Medical Association. Dr. Holman served in the R.A.M.C. throughout the last war, attaining the rank of lieutenant-colonel, and was appointed O.B.E. in 1944 for gallant and distinguished services in Italy. On his return to civilian life he went to live at Stanmore, soon afterwards accepting an appointment as medical officer with the North Thames Gas Board.

W. G. writes: To a multitude of friends the untimely death of Geoffrey Holman will bring a sense of loss and bewilderment. In this age, when few seem to have much zest for living, he was an outstanding exception. Medicine, sport, gardening, good food, good wines, the love of children, and the study of his fellow men excited and held his abiding interest. Born and bred in a medical family—for nearly a hundred years before 1939 a Holman had practised medicine in St. John's Wood—he was at his best as a family doctor. In that sphere his sound clinical sense, kindness of heart, and sense of humour endeared him to a large number of patients of all ages in all walks of life. Although after the war circumstances turned his steps to industrial medicine he never seemed to find that more impersonal sphere completely satisfying. His war record was revealing. He volunteered for the Army in July, 1939, and served in the R.A.M.C. until 1945. Posted overseas in the winter of 1939–40, he survived the perils of Dunkirk, and after service in Madagascar and India eventually commanded the

141st Field Ambulance during the Italian campaign. There he earned the confidence and affection of all ranks, and for his distinguished services in the field was awarded the O.B.E. Later, in the Central Mediterranean Training School, he was outstandingly successful as senior instructor. Men of the calibre of Geoffrey Holman are rare beings, and to his devoted wife and children goes the sympathy of all who knew him.

The many friends and patients of Dr. T. CARLYLE MITCHELL heard with dismay of his sudden death from coronary thrombosis on October 18, St. Luke's Day. He was 51, and had that morning, as was his wont, attended mass with his family. He felt unwell at lunch-time, but was determined to attend an afternoon meeting of the Radlett Rifle Club, of which he was a founder and leading member. On reaching the firing point he again felt unwell and was returning to his car, when he collapsed and died shortly afterwards. Born in Natal, South Africa, on October 2, 1902, Thomas Carlyle Mitchell studied medicine at Edinburgh University, graduating M.B., Ch.B. in 1927. He proceeded to the M.D., with high commendation, two years later, being awarded the Syme surgical fellowship for his thesis. In 1930 he became M.R.C.P.Ed. and won the Grocers' Company's medical research scholarship, and he was elected a Fellow of the College in 1936. After graduation he held the appointments of house-physician and house-surgeon at Chalmers Hospital, Edinburgh, before going back to South Africa to become resident medical officer at Grey's Hospital, Pietermaritzburg. He returned to England in 1934 and was in practice at Norwood, where he was honorary surgeon to the Norwood and District Cottage Hospital, and later at Rugby and Mill Hill, before settling at Radlett in 1943. At the time of his death he was on the medical staff of the Bushey and District Hospital.

E. J. C. writes: Dr. Mitchell was an active member of the West Herts Division of the British Medical Association, and many a remark made or question asked by him at meetings was well worth attention. He was a man of few words, always well chosen, and of great integrity. His death left a sense of bewilderment among his patients, to whom he was not only a trusted medical adviser but a real friend. His colleagues will miss him sadly, and our sympathy goes out to his widow and his four sons and three daughters. I was privileged to know him at home, and never was there a happier family. His indeed was a life fully spent in the service of others. This was evidenced by the large congregation at the requiem mass at the memorial service held in Christ Church, Radlett.

Medico-Legal

CONTAMINATED SPINAL ANAESTHETIC

Mr. Justice McNair, in the Queen's Bench Division on November 12, gave judgment for the defendants in an action in which two former labourers alleged that they became paralysed from the waist downwards following the administration of spinal anaesthetics when they were operated upon at Chesterfield Royal Hospital on October 13, 1947.

The men, Mr. C. H. Roe, aged 51, and Mr. A. Woolley, aged 62, claimed damages from the Ministry of Health, as successors to the former trustees of the hospital, and Dr. J. Malcolm Graham, the visiting anaesthetist. Plaintiffs alleged the anaesthetic was negligently administered, and contended that their paralysis was caused by the phenol solution in which the ampoules were immersed before their operations.

The allegations were denied.

Ciba Laboratories, Ltd., manufacturers of "nupercaine," the anaesthetic, who appeared as third defendants, were dismissed from the action earlier as having no liability.

Expert Evidence

Professor R. R. Macintosh, consultant anaesthetist, giving evidence for the plaintiffs, said the best method of sterilizing ampoules was by autoclaving. He had used nupercaine for spinal anaesthetics and did not think the anaesthetic caused the paralysis. He thought the paralysis was caused by phenol.

Professor Brodie Hughes, professor of neurosurgery in the University of Birmingham, said that, if sufficiently concentrated, phenol would kill the nerve cells. He said it was a practice in 1947 to store ampoules in phenol. He knew before 1950 that it was possible for spirit to seep into ampoules through cracks not visible to the naked eye. In cross-examination he agreed that it was an accepted practice in Britain in 1947 to store ampoules in antiseptic solutions.

Dr. J. Carson, consulting neurologist, giving evidence for the plaintiffs, said he examined them in 1947; he thought the spinal injection caused the paralysis, and the most probable cause was a chemical irritant.

Sir Francis Walshe, consultant neurologist, giving evidence for the Ministry, said the plaintiffs' injuries were consistent with the use of spinal anaesthetics. He said their case histories were inconsistent with a corrosive poison such as phenol. If phenol had been responsible, he would have expected it to be dramatic at the onset and immediate in its effect.

Dr. Macdonald Critchley, consulting neurologist, said he thought the plaintiffs' condition was a most intense form of complication due to spinal anaesthetics. Their condition was typical of what was known to follow the administration, at times, of spinal anaesthetics.

Sir Hugh Griffiths, consulting surgeon, called for the Ministry, said he thought the plaintiffs' condition was caused by the anaesthetic injection.

Administration Perfectly Normal

Dr. Graham said he had given about 500 spinal anaesthetics before October, 1947. Mr. Roe's operation was performed in the morning and Mr. Woolley's in the afternoon. The first indication he had of anything abnormal was when Mr. Roe complained of a headache during the operation. It was not until three days later that he knew something was seriously wrong. He said that in the case of Mr. Woolley the administration of the anaesthetics was perfectly normal. He had no idea what had happened to the plaintiffs until Dr. Carson had visited the hospital. In 1947 he did not appreciate the danger of phenol penetrating an ampoule through an invisible crack. Some weeks before the operation he had found a cracked ampoule in the phenol solution, and rejected it. He spotted it at once. He denied that he casually examined the ampoules.

Dr. R. W. Cope, consulting anaesthetist, said that ampoules could be contaminated through invisible cracks. He did not think an ordinary competent anaesthetist would appreciate that in 1947.

Judgment

Mr. Justice McNair, giving judgment, said the operations on Mr. Roe and Mr. Woolley were comparatively minor, but in each case the result was disastrous: both unfortunate men were now permanently paralysed from the waist downwards. The method of anaesthesia was in 1947 a well-known method, and no charge of negligence had been made in regard to the adoption of that method in these two cases.

The hospital's obligation was to provide a competent anaesthetist, which obligation it had undoubtedly fulfilled. In his lordship's view a specialist anaesthetist was in the same class as a visiting surgeon, and the hospital did not assume responsibility in law for his acts. Although Dr. Graham was responsible for the choice of anaesthetic and the activities of the theatre staff, he could not be regarded as being responsible for any of their casual acts of negligence. The hospital was responsible for any acts of negligence by the theatre staff on the basis of master and servant.

The judge said he found that the plaintiffs' injuries were in fact caused by contamination of the nupercaine by phenol. The percentage of such injuries following such anaesthesias seemed to be about 1 in 10,000. An explanation that in those rare cases the injuries were due to some personal

idiosyncrasy of the patient was difficult to accept in these particular cases because the injuries to Mr. Roe and Mr. Woolley resulted from the same anaesthesia injected by the same anaesthetist on the same day. That seemed to point conclusively to some common factor in the two cases. Phenol was present in the theatre, because the glass ampoules containing the nupercaine were stored in a phenol solution of 1 in 40, after a temporary immersion in a solution of 1 in 20. Glass ampoules could crack, and if they did there might be a replacement of nupercaine by phenol, although the measure of replacement might not be capable of being noticed. In his lordship's opinion, therefore, phenol was the most likely common factor.

It was now clear that phenol could find its way into the ampoules through invisible cracks, but in 1947 the ordinary general run of anaesthetist would not appreciate that risk. The judge continued: "I accordingly find that by the standard of knowledge of competent anaesthetists in 1947 Dr. Graham was not negligent in failing to appreciate this risk." He also found that the theatre staff were not negligent.

His lordship added that, having seen Dr. Graham and heard him give his evidence in a forthright manner, he found it extremely difficult to believe he could have missed two visibly cracked ampoules. Plaintiffs' claim against the Ministry and Dr. Graham failed, and there would be judgment for both defendants.

Defendants did not ask for costs against the plaintiffs and no order was made as to costs.

Messrs. Hempsons acted on behalf of the Medical Defence Union for Dr. Graham.

Medical Notes in Parliament

N.H.S. Fog Masks

The Minister of Health announced on November 13 his decision to permit the prescribing of specified types of fog mask for issue under the Health Service. The regulations he was making that day, he said, would become effective on November 17 and masks should normally be available from that date. Similar arrangements would be made in Scotland.

Mr. IAIN MACLEOD, answering a question by Mr. F. GOUGH, said he was advised that in the present state of knowledge no mask which people could be expected to wear for long periods was likely to give complete protection, but that there were certain types of mask which might give some help to people suffering from existing disease of the heart or lungs. He was therefore proposing to enable doctors, if they felt it to be desirable in each individual case, to prescribe under the National Health Service certain specified types of mask for patients suffering from these conditions who lived or worked in an area where smoke-polluted fog was likely to occur.

The combination of intense fog and cold which occurred in London last December had been an extremely rare occurrence. It was, however, important not to confuse it with the more normal fogs with which we had long been familiar, nor to exaggerate its effect on normal healthy people. The long-term problem was that of the removal of the causes of pollution, and this was being studied by a committee under the chairmanship of Sir Hugh Beaver. This was appointed by the Minister of Housing and Local Government and the Minister of Fuel and Power, and would report shortly.

Fees for Cremation Certificates

Mr. J. REEVES asked the Home Secretary for a statement on the high fees charged by medical practitioners for certificates required under the Cremation Acts. Sir DAVID MAXWELL FYFE stated that the British Medical Association had advised medical practitioners that a suitable fee for the completion of either Certificate B or Certificate C was two guineas plus a mileage allowance, where applicable, at the rate of 1s. per mile or part of a mile each way outside a radius of two miles. In view of this action he did not propose at present to make use of the power contained in the Cremation Act, 1952, to prescribe maximum fees.

Proprietary Medicines

Dr. BARNET STROSS, on November 12, asked the Minister of Health how many medical preparations listed in the *National Formulary* were dearer than the proprietary brands of the same preparations, and whether he would list them. Mr. IAIN MACLEOD replied that of preparations in common use in general practice the cost to the Health Service of eighteen was greater than that of their proprietary equivalents. Ten others might in some circumstances be dearer according to which of the equivalent products was prescribed or the size of the pack from which it was dispensed. These eighteen were :

Tab. mepyramin. maleat. *N.F.* 100 mg. Tab. succinylsulphathiazol *B.P.* Tab. pethidin. hydrochlor. *B.P.* 50 mg. Tab. aethinyloestradiol. *B.P.* 0.05 mg. Tab. ethinyloestradiol. *B.P.* 0.1 mg. Tab. ergotamin. tart. *B.P.C.* Tab. ferr. sulph. co. *B.P.C.* Tab. oestron. *B.P.* 1 mg. Tab. aethisteron. *B.P.* 5 mg. Tab. acetarsol. *B.P.* 4 gr. Tab. stilboestr. *B.P.* 0.5 mg. Tab. promethazin. hydrochlor. *N.F.* 10 mg. Tab. amidon. hydrochlor. *B.P.C.* Tab. butobarbiton. *B.P.C.* Tab. phthalylsulphathiazol. *B.P.C.* Tab. sulphadimidin. *B.P.* Tab. hexoestr. *B.P.* 1 mg. Tab. thyroid. *B.P.* ½ gr.

Dupuytren's Contracture

Mr. FENNER BROCKWAY asked the Minister of Pensions and National Insurance on November 9 if he would add Dupuytren's contracture to the list of industrial diseases entitled to compensation under the Industrial Injuries Act. Mr. OSBERT PEAKE refused, stating that on the evidence available he was not satisfied that it fulfilled the conditions for prescription laid down in the Act. He added in further replies that the general question of the prescription of industrial diseases was before the Beney Committee. He was assured by his medical advisers that this particular disease was primarily constitutional in origin.

Dr. BARNET STROSS said that those who had been most concerned with this type of ailment were satisfied that the Minister was being wrongly advised, and that, in addition to a constitutional factor, when the histories were considered carefully it was found that there was always a precipitating factor due to injury. He mentioned the case of a dancing master who suffered from it, the cause being that he used a file constantly for two years in another occupation at the age of 20. Mr. PEAKE expressed his willingness to receive details of the case.

T.A. Doctors' Car Allowance

Mr. READER HARRIS asked the Secretary of State for War on November 10 if he was aware that the amount of the allowance for use of their own cars on Army business by doctors doing Territorial Army Service was inadequate; and if he would increase the allowance so that such doctors were not out of pocket. Mr. A. HEAD said that he had already had evidence that certain of the present rates were causing dissatisfaction and he was giving consideration to that problem.

Work for the Disabled

Mr. HAROLD WATKINSON, Parliamentary Secretary, Ministry of Labour, stated on November 10 in answer to Mr. J. SIMMONS that the number of disabled persons unemployed had fallen steadily throughout the first seven months of this year. Despite some increase in the following three months it was now lower by more than 9,000 than it was in January. This included a substantial reduction among the older workers. The Ministry would continue to do all it could to reduce the number still further.

Treatment of Chronic Diseases

Mr. R. T. PAGET initiated a debate on November 13 on the care and treatment of the chronic sick. Mr. LESLIE HALE said that Dr. C. R. Lowe and Professor T. McKeown had shown in the Birmingham region that about one-tenth

of the total available number of hospital and infirmary beds was required for the treatment of patients over 65. The report of the Bristol Local Medical Committee was a model report on the care of the chronic sick in Bristol. It stated, among other things, that a mobile physiotherapy service was operating on a voluntary basis, but was handicapped by lack of funds and the opposition of the Ministry of Health to mobile services working under general-practitioner control. Referring to diseases of the central nervous system, which he said appeared to be on the increase, he suggested that one of the wartime aerodromes could be adapted for the accommodation of patients, and would so used provide a "laboratory" for the research so essential in these diseases, particularly Parkinson's disease and disseminated sclerosis.

Miss PAT HORNSBY-SMITH, in the Government reply, stated that the number of beds for the chronic sick in the Health Service hospitals had risen from 50,300 to 54,000, and the number of contract beds in institutions from 538 to 1,754. There had also been a marked increase in the treatment made available in out-patient departments, particularly in physiotherapy, where the number of patients had risen from 2,210 in 1950 to 6,071, with total attendances of 26,247. But the waiting-lists also had continued to increase, and were now approximately 9,000. One cheering figure that had emerged in the last two years was that they were getting a better turnover of patients who needed close attention by increasing rehabilitation. Considerable progress had been made in the geriatric service, about 60 units were in operation, and the specialist geriatricians recently appointed in many of the regional areas had concentrated their efforts on rehabilitation.

About the controversy in Bristol, where some G.P.s wished to provide a physiotherapy service, she said it was within the power of the practitioner to direct that a patient should enjoy the far wider facilities available in the hospitals. The Ministry felt that the best service they could provide was under a consultant in a hospital rather than by a small mobile unit. The question of cover for diseases under the Industrial Injuries Act was under review by a departmental committee with Mr. Beney as chairman. Its terms of reference were to review the provisions of the Act on which benefit was paid for industrial diseases and injury not caused by accident, and to make recommendations.

Rock Carling Investigation

Mr. OSBERT PEAKE, Minister of Pensions and National Insurance, on November 16 informed Mr. JAMES SIMMONS that he had not yet received the final report of the Rock Carling Committee. The special examination of several thousand pensioners for which the committee had asked was taking longer than was expected. The committee, composed almost entirely of doctors, disagreed among themselves. As a result the examination of some 4,500 men was undertaken. They wanted it to be a thorough examination, because the results would be of world-wide importance.

Universities and Colleges

UNIVERSITY OF EDINBURGH

At a Graduation Ceremonial on July 15 the following degrees and diplomas were conferred:

M.D.—[1]Barbara E. Clayton, [1]G. Dempster, H. J. Gibson, I. D. Grant, [2]A. A. Guild, M. W. MacD. Hadley, [1]G. B. Ludlam, [1]E. W. Macmillan, M. MacM. Macrae, [2]D. MacVicar, [1]I. M. Richardson, [1]R. F. Robertson.

PH.D.—*In the Faculty of Medicine:* [2]F. A. Hamdi, M.B., B.Ch., [2]F. L. W. Jayewardene, M.B., B.S., K. Mahadeva, L.M.S., [2]B. G. Ray, M.B., B.S.

M.B., CH.B.—W. L. Aikman, C. J. Barton, Violet M. MacD. Campbell, Mary B. Jamieson, S. S. S. Keys, J. A. King, N. McKerrow, I. Maclachlan, N. L. McMillan, J. B. McWhinnie, Margaret B. Manson, D. R. B. Mends, Harriet R. Mitchell, D. N. Nicolson, J. W. Sandison, A. J. Simpson, F. J. Smyman, Sheila C. Spark, K. M. Stewart, G. J. Whiston.

DIPLOMA IN PUBLIC HEALTH.—P. E. Brown, W. R. Brown, A. R. Duff, Lucy McL. C. B. Duncan, J. H. Fox, I. G. P. Fraser, Eleanor J. More, R. J. A. Morris, W. O. Petrie, I. B. Sutherland, Margaret H. F. Turnbull, R. L. Walsh, H. G. H. Waters.

DIPLOMA IN MEDICAL RADIODIAGNOSIS.—J. M. Brunton, N. T. Spiers.

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—P. Crosby, Elizabeth A. De Rose, N. S. Ghani, C. W. G. Irvine, D. L. Mackay, K. P. N. Pai, K. Parameswaran, J. F. Rodrigo, M. Tajuddin.

The following scholarships, bursaries, prizes, etc., were awarded in the Faculty of Medicine: *Royal Victoria Hospital Tuberculosis Trust Medal*, S. S. S. Keys. *George Guthrie Research Fellowship in Child Health*, I. C. Lewis. *Paterson Travelling Scholarship in Surgery*, Sir James D. Fraser. *Crichton Research Scholarship*, R. B. Duthie. *Gunning Victoria Jubilee Prize in Materia Medica*, C. W. M. Wilson. *Wellcome Medal and Prize in the History of Medicine*, J. J. McKessack. *Wightman Prize in Clinical Medicine*, A. W. McKenzie. *Maclagan Prize in Forensic Medicine*, C. J. W. Huston. *Stirton Bursary* and *Colonel Thomas Biggam Memorial Medal and Prize in Pathology*, Elizabeth M. Connell. *Gunning Medical Bursaries*, D. C. Flenley, I. B. Macleod, R. J. Wilson. *George William Falconer Macnaughton Bursary in Physiology*, D. P. Braid. *Senior John Aitken Carlyle Bursary in Anatomy and Physiology*, T. W. Fenton. *Junior John Aitken Carlyle Bursary in Anatomy and Biochemistry*, W. J. Irvine; *proxime accessit*, J. A. Birkbeck and W. A. Souter. *Mackenzie Bursaries in Anatomy*, W. J. Irvine, Jean M. D. Dott, W. A. Souter; and G. M. Paterson and Phyllis M. Fulton (equal). *Whiteside Bruce Bursary*, W. Simpson. *Ross Inkster Medal in Public Health and Social Medicine*, Elizabeth L. Jamieson. *Lewis Cameron Undergraduate Prize in Bacteriology*, H. A. Crispin and M. G. Kerr (equal). *Cunningham Memorial Medal and Prize in Anatomy*, I. B. Macleod. *Ian Oswald Prizes in Anatomy*, J. A. Waddell, T. W. Fenton. *Robert Wilson Memorial Prize in Chemistry* and *Vans Dunlop Prize in Physics and Chemistry*, H. G. Coore. *Boots Drummond Memorial Prize in Biochemistry*, R. J. Wilson. *Vans Dunlop Prize in Botany and Zoology*, Sadie D. Walsh and Lilian L. Orba (equal). *MacGillivray Prize in Zoology*, Sadie D. Walsh.

[1]Highly commended for thesis. [2]Commended for thesis. [3]*In absentia.*

UNIVERSITY OF LIVERPOOL

The following candidates have been approved at the examinations indicated:

M.D.—J. H. E. Carmichael, J. C. Davis, F. Lanceley, G. McLoughlin, A. L. Smallwood, Esme M. Wren.

CH.M.—D. Annis, E. W. Parry.

PH.D.—*In the Faculty of Medicine:* A. H. Cruickshank, M.D.

FINAL M.B., CH.B.—Mary F. Allen, D. H. Alltree, Audrey Beavan, Joyce V. Blackburn, Marjorie J. Bowness, Margaret M. Bradley, Cicily G. Brenner, W. G. Cooper, I. G. Currie, Diana M. F. Daniel, Muriel Douglas, O. Dworetzki, A. Dyson, K. B. Edwards, Elizabeth E. Evans, Shirley R. Fine, Margaret K. Flenley, D. C. French, R. W. Galloway, [1]Elizabeth M. Grantham, H. Halsall, Sylvia Hawthorne, D. Helbert, P. G. Holt, L. Horwich, Eileen M. Howarth, J. C. Jaques, Nuala M. Kelly, J. H. Leavesley, Ann B. Lewin, Pamela R. Lipman, Eleanor C. Lloyd, I. L. Loch, Ursula Loewenthal, P. F. Lynch, [1]Kathleen T. McCurley, Joan E. McFarland, Kathleen McKee, G. M. Makhlouf, G. M. Mason, R. Middlefell, R. Owen, M. Pearson, C. R. Porteous, E. J. Raffle, A. Ramsden, Le R. H. Le Riche, Cynthia R. Roberts, G. S. Roberts, J. H. Roberts, J. S. Robinson, R. W. Rouse, P. J. W. Rowell, J. H. Rustage, R. T. Shepherd, R. I. Smith, [1]S. E. J. Smith, Gwladys E. P. Williams, Mary B. Woodfield, S. J. P. Woods, Helen E. Worsley, P. J. J. Wren, V. Wright. *Passed in separate subjects:* S. J. Alltree, D. F. Rice (surgery and obstetrics and gynaecology), D. R. Cole, T. R. W. Cowell, M. A. R. Eslick, C. D. Fisher, D. N. Guest, D. R. Morris, A. M. Stewart (medicine and surgery), L. M. Ellis, F. Hewitt, I. V. Lishman, S. Naylor (medicine and obstetrics and gynaecology).

DIPLOMA IN PUBLIC HEALTH.—Catherine M. Connolly, Alice T. McGlinchey, J. McHugh, A. N. Pickles, W. A. Pollitt, L. G. Poole, Z. D. A. Sheikh, C. Sudhipongse, T. Sukhanenya, Sheila M. Towers.

DIPLOMA IN RADIOLOGY.—*Radiodiagnosis:* A. Ansell, G. Ansell, P. K. Ganguli, R. I. Green.

FINAL M.B., CH.B.—*Part I:* J. L. Crane, E. E. Cureton, G. Horne, T. Owen. *Part II:* I. K. Brown, D. V. Coakley, W. P. Cuthbert, W. A. Downie, G. O. Dubourg, M. W. Fowles, S. G. Gooch, Brenda Grant, H. G. Harding, Gladys E. Hemes, E. Holmes, T. R. T. Hughes, J. B. McFarland, J. L. Mason, J. B. Peters, W. V. N. Pugh, R. W. Royston, T. Trace, E. S. Wylie, R. A. Yorke.

[1]With distinction in obstetrics and gynaecology.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **October 31** (No. 43) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES In Countries and London	1953					1952				
	Eng. & Wales	Lond	Scot	N. Ire	Eire	Eng. & Wales	Lond	Scot.	N. Ire	Eire
Diphtheria	18	0	5	0	2	28	1	8	0	2
Dysentery	394	56	219	1	1	236	13	83	2	1
Encephalitis, acute	3	1	0	0		3	1	0	0	
Enteric fever:										
Typhoid	4	3	2	0		8	0	0	0	
Paratyphoid	8	2	5	0		8	0	2(B)	0	
Food-poisoning	113	7		5		64	9		0	
Infective enteritis or diarrhoea under 2 years				9	36				21	34
Measles*	842	12	27	14	49	9,178	1094	139	42	123
Meningococcal infection	22	1	12	0	1	21	1	19	1	2
Ophthalmia neonatorum	39	3	6	0		29	3	9	0	
Pneumonia†	526	35	156	7	1	519	46	251	8	3
Poliomyelitis, acute:										
Paralytic	88	12	30	6	8	75	3	5	1	4
Non-paralytic	34	2				26	1			
Puerperal fever§	245	20	8	0		251	22	11	1	
Scarlet fever	1,226	87	235	38	66	1,994	200	360	27	103
Tuberculosis:										
Respiratory			156	25				135	35	
Non-respiratory			21	6				25	4	
Whooping-cough	2,067	98	295	46	86	1,206	77	106	26	65

DEATHS In Great Towns	1953					1952				
	Eng. & Wales	Lond.	Scot	N. Ire	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0		0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0		0	
Infective enteritis or diarrhoea under 2 years	6	0	1	0	0	9	1	1	0	1
Influenza	15	1	0	0	0	10	2	3	0	1
Measles		0	0	0	1		0		0	0
Meningococcal infection		0	0				1			
Pneumonia	188	20	12	5	5	205	36		4	4
Poliomyelitis, acute	2	0	1		0	4	0			0
Scarlet fever		0	0	0	0		0		0	0
Tuberculosis:										
Respiratory	90	12	12	3	2	97	10	18	0	5
Non-respiratory		0	1	1	2		3	3	0	3
Whooping-cough	4	1	0	0	0	2	0		0	0
Deaths 0–1 year	212	21	23	6	12	233	29	30	6	16
Deaths (excluding stillbirths)	4,930	707	526	115	159	5,154	770	540	118	171
LIVE BIRTHS	6,957	1040	864	185	391	7,061	1056	838	209	396
STILLBIRTHS	170	27	23			208	32	24		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Census Report on London

The population of the County of London at the 1951 census was 3,347,982, representing a net decline over the whole period since the 1931 census of over a million persons, most of which has occurred since 1939. The population enumerated in the City of London was 5,324 persons as compared with 10,999 in 1931.

The dwellings occupied by private households or vacant numbered 820,918. Since the 1931 census some 100,000 new permanent dwellings have been erected, nearly one-third being post-war; some 70,000 have been totally destroyed by bombing during the war; and 30,000 new dwellings have been added since the war as a result of conversions.

There has been a reduction in the density of occupation of dwellings from 0.98 persons per room in 1931 to 0.83 per room in 1951. The percentage of persons living at over two persons per room has declined for the county as a whole from 13.1 in 1931 to 2.5 in 1951, the incidence of such conditions now affecting less than 5% of the population in private households in every borough (except Paddington with 5.2%). The wide variations in this respect which prevailed in 1931, when there were 7 boroughs with over 20% of population living at densities of over two persons per room, have thus been eliminated.

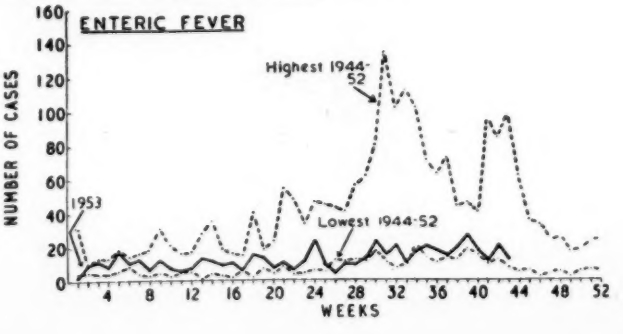
A third of all private households in the county have exclusive use of piped water supply, cooking stove or range, kitchen sink, water closet, and fixed bath; and another 20% have all except a fixed bath—that is, 62% of the households do not have exclusive use of a fixed bath. The incidence of households entirely without is highest in the boroughs of central and eastern London.

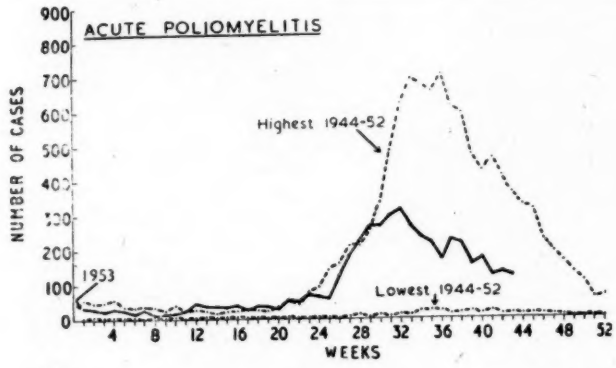
There is not much difference in the age composition of the country as a whole and the County of London, and the proportion of persons aged 65 and over (11.1%) is the same in London as in the country as a whole. The number of females per 1,000 males in the County of London is now 1,138. The ratio is much higher in some of the areas which house disproportionately large numbers of single persons living alone; thus Chelsea shows 1,402, Hampstead 1,390, Kensington 1,332, and St. Marylebone 1,396 females per 1,000 males.

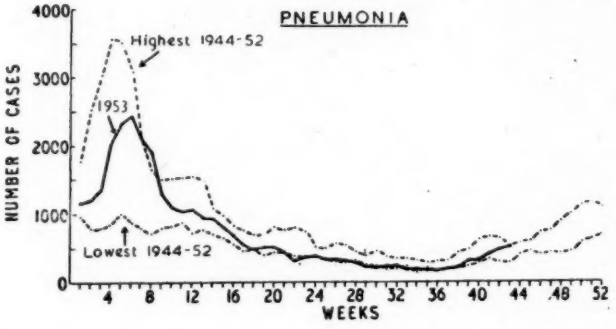
There is a higher proportion of men in social class I in London (as also in the south-eastern region) than in the country generally, this reflecting the concentration in the metropolis of persons in the professional, administrative, and managerial grades.—*Census 1951: County Report, London* (H.M.S.O., 22s. 6d.).

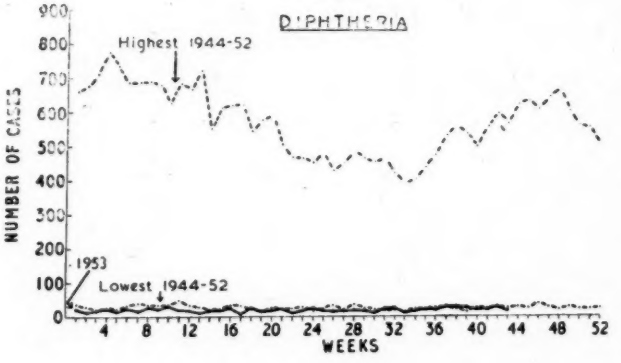
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - -, the figures for 1953 thus ————. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

Only small variations occurred in the trends of infectious diseases in England and Wales during the week ending October 31. The largest were decreases in the number of notifications of 123 for whooping-cough, from 2,190 to 2,067, and 43 for scarlet fever, from 1,269 to 1,226, and increases of 84 for dysentery, from 310 to 394, and 51 for pneumonia, from 475 to 526.

The decrease in the incidence of scarlet fever was due to two counties—Lancashire with a fall of 48 in the number of notifications, from 194 to 146, and Yorkshire West Riding with a decrease of 45, from 190 to 145. Only very small changes occurred in the incidence in other counties, though there was a small rise for the whole of the southern section of the country. The largest falls in the number of notifications of whooping-cough were 58 in Yorkshire West Riding, from 248 to 190; 35 in Essex, from 149 to 114; and 32 in London, from 130 to 98: and the largest rises were Staffordshire 43, from 91 to 134; and 37 in Lancashire, from 179 to 216. 842 cases of measles were notified, 19 fewer than in the preceding week. The largest variations in the local returns were an increase of 46 in Staffordshire, from 60 to 106, and a decrease of 45 in Lancashire, from 250 to 205. 18 cases of diphtheria were notified, being 11 fewer than in the preceding week. All but 2 of the cases were notified in two counties; the centres of infection were 9 in Staffordshire (Coseley U.D. 7) and 7 in Lancashire (Liverpool C.B. 4).

122 cases of acute poliomyelitis were notified during the week; these were 1 fewer for paralytic and 12 fewer for non-paralytic cases than in the preceding week. The largest returns were Lancashire 21 (Liverpool C.B. 6), London 14 (Lewisham 7), Yorkshire West Riding 10, Staffordshire 7.

The rise in the notifications of dysentery was contributed by Yorkshire West Riding and Lancashire. In the former county the cases were 53 and in the latter 27 more than in the preceding week. The largest returns were Yorkshire West Riding 93 (Bradford C.B. 68), Lancashire 64 (Bolton C.B. 31), London 56 (Chelsea 14), Yorkshire North Riding 34 (Middlesbrough C.B. 34), Essex 15 (Ilford M.B. 9). In Scotland the largest centres of dysentery were Glasgow 82, Lanark County 48, and Edinburgh 25.

Week Ending November 7

The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,187, whooping-cough 2,175, diphtheria 18, measles 1,030, dysentery 358, acute poliomyelitis 94, paratyphoid fever 9, and typhoid fever 3.

Medical News

Chair of Rheumatology at Manchester.—Manchester University has established the first chair of rheumatology in Britain. The University was able to do this following a generous offer by the Empire Rheumatism Council to provide £3,000 yearly towards the cost. The first holder will be Dr. J. H. Kellgren, at present reader in rheumatic diseases and director of the rheumatism research centre at Manchester University. Dr. Kellgren will take up his new appointment at the end of December.

Smog Masks.—General practitioners may now prescribe under the N.H.S. special masks for use in smog "when the wearing of a mask is a necessary part of treatment during exposure to smoke-polluting fog of a patient who is suffering from cardiac disease or respiratory disease." There are two types of mask. One is a semi-rigid frame holding a removable thin gauze and cotton tissue pad and fitting closely to the cheeks (cost 2s. 5d.). The other is made of muslin shaped to cover nose and mouth and carrying shaped removable thin gauze and cotton tissue pads (cost 1s. 1½d.). The regulations under which these masks may be prescribed came into force on November 17 and preclude the prescribing of masks for healthy people.

Local Medical Societies.—Recent meetings have included the following: *Manchester Medical Society.*—On October 7 Professor John Morley delivered his presidential address to the society, taking as his subject "A Surgical Retrospect." He described some of the features of life in the old Royal Infirmary in the centre of Manchester when he was a student and house-surgeon. In those days surgeons took a far too mechanical view of functional disorders of the abdomen, trying to cure them by "slinging-up" operations. Nowadays such cases would be regarded as being due to an anxiety state and be treated by a psychiatrist. On October 13 Mr. O. M. Duthie addressed the Section of Surgery on retinal detachment. He ended his lecture with a film illustrating the technique of surface diathermy followed by inter-retinal puncture and injection of the vitreous with saline. On October 26 Dr. R. W. Fairbrother gave a paper to the Section of General Practice on antibiotic therapy. He emphasized the increasing tendency to use combinations of antibiotics, but said that there was little to justify this in the case of a single infection. "There is little evidence that synergistic action actually occurs; indeed, in a few instances interference of one antibiotic by another has been demonstrated." *North of England Otolaryngological Society.*—This society held a successful meeting on October 10, when a variety of interesting clinical cases were shown. *Medical Society of London.*—In the course of his presidential address on the significance of haematuria, delivered on October 12, Mr. E. W. Riches

declared that nephritis was not a common cause of visible blood in the urine. When there was macroscopic haematuria a new growth would be found in the urinary tract in more than half the cases. Painless haematuria was usually of graver import than a painful haematuria. *Chelsea Clinical Society.*—This society held its opening meeting on October 13, when Dr. Eliot Slater, Dr. Desmond Curran, and Sir Ernest Gowers began a discussion on the M'Naghten Rules. *Liverpool Medical Institution.*—On October 14 there was a symposium on the "Use and Abuse of Antibiotics." On November 5 the management of paraplegia was discussed. Mr. A. Sutcliffe Kerr, in opening the proceedings, stressed the great importance of transferring cases of traumatic paraplegia to a special centre at the earliest possible moment, so that they could receive the highly skilled attention necessary for the prevention of pressure sores and urinary complications. Such patients were ready for discharge home in from six to twelve months. Mr. Cosbie Ross reported that he had carried out bilateral pudendal neurectomy in 20 patients who had spastic obstruction of the bladder sphincters, as diagnosed by cysto-urethrography, and the results had been good.

Hadfield Report on General Practice.—In this month's issue of the *Medical World* there is a "critical assessment" of Dr. S. J. Hadfield's "Field Survey of General Practice, 1951–2" (*Journal*, September 26, p. 683) by Dr. S. J. Collings. According to a leading article in the same journal, Dr. Collings's contribution was by invitation. Dr. Collings, an Australian, was the author of a report entitled "General Practice in England To-day: a Reconnaissance" (*Lancet*, March 25, 1950, p. 555), which he wrote after a year's study of some general practices in this country.

Royal Medal.—Sir Paul Fildes, F.R.S., formerly director of the Medical Research Council's bacterial chemistry research unit, has been awarded one of the Royal Society's two Royal Medals for the year. According to the citation, the award is for "his classical researches on growth factors for bacteria and for laying the foundation of work leading to a rational approach to chemotherapy." The medal is given with the approval of the Queen on the recommendation of the Council of the Royal Society.

Annual Meeting at Toronto.—The arrangements for the Joint Annual Meeting with the Canadian Medical Association to be held in Toronto in 1955 were described in the *Journal* of November 7 (p. 1055). It should be noted that the figure given for the cost of a return ticket by air in one direction and by sea in another was incorrect. Such a ticket will cost approximately £225 first-class and £165 tourist. Those members who are thinking of attending the Meeting are invited to inform the Secretary of the Association of their intentions or provisional intentions as soon as possible. It is particularly important that the numbers of those wishing to accept the offer of private hospitality in Toronto should be approximately ascertained at an early date, and it will be helpful if an indication could be given of the travel arrangements preferred.

Fullbright Travel Grants.—Under the Fullbright programme, grants for travel to the United States between June, 1954, and April, 1955, are available to citizens of the United Kingdom and Colonies who are going to America for study, research, or lecturing. These awards are competitive and are limited to holders of a degree or recognized professional qualification who have been accepted at an American institution of higher learning. The grants are not available for maintenance expenses while in America. Further information about the grants may be obtained from the United States Educational Commission in the United Kingdom, 55, Upper Brook Street, London, W.1.

Family Planning Association.—The second medical conference of the Family Planning Association was held in London on November 7, and attended by 85 doctors. One of the subjects discussed was a chemical spermicide which is claimed to be an effective contraceptive when used without any mechanical barrier. Dr. Margaret Hadley Jackson, presenting the association's attitude, said that the evidence so far was that there was no chemical preparation which by itself gave adequate protection to the woman who must not have another baby. Other speakers confirmed this view.

Prize for Research on Addiction.—The Society for the Study of Addiction announces the establishment of a Hubert Norman Prize of 100 guineas to stimulate research into the causation and prevention of addiction. The first prize will be for a "study or investigation of substances, other than 'antabuse' or its derivatives, causing distaste, disinclination, or dislike for alcohol." The prize is open to both medical and non-medical workers throughout the world. The last date for the receipt of entries is December 31, 1954. Further details may be obtained from the Editor, *British Journal of Addiction*, 34, Addison Road, London, W.14.

Midwives.—On March 31 this year there were 56,678 midwives on the Midwives Roll, an increase of 1,838 on the preceding year. Of these, however, only 17,472 notified their intention to practise.

Sir Alexander Fleming, F.R.S., was among those who received the honorary degree of LL.D. at the hands of the Duke of Edinburgh on November 4, the occasion of the Duke's installation as Chancellor of Edinburgh University.

COMING EVENTS

Heberden Oration.—Sir Russell Brain, P.R.C.P., will deliver the oration on December 4 at 3.30 p.m. at the Royal College of Surgeons. He will speak on "Spondylosis: The Known and the Unknown."

An International Congress of Clinical Pathology will be held in Washington, U.S.A., from September 6 to 11, 1954. All inquiries regarding the Congress should be addressed to Dr. R. A. Moore, Washington University School of Medicine, 660, South Kingshighway, Saint Louis 10, Missouri, U.S.A.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Monday, November 23

INSTITUTE OF NEUROLOGY.—5 p.m., Professor P. Nayrac (France): **Wilson's** Disease.

MEDICAL SOCIETY OF LONDON.—8.30 p.m., discussion to be introduced by Dr. Robert Forbes: Lessons from Recent Litigation Against Registered Medical Practitioners.

●POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. Raymond Daley: Problems in Connexion with Pulmonary Hypertension.

Tuesday, November 24

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor H. L. Sheehan: Vascular Lesions of Pituitary Necrosis.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. G. B. Dowling: Tuberculosis of the Skin.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 3 p.m., Professor James Young: Maternity in Great Britain.

LIVERPOOL MEDICAL INSTITUTION.—8 p.m., Florence Blair-Bell Memorial Lecture by Professor G. R. Cameron, F.R.S.: Liver as the Site and Source of Cancer.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—3.45 p.m., Erasmus Wilson Demonstration by Dr. L. M. Franks: Benign Enlargement and Precancerous Hyperplasia in the Human Prostate.

ROYAL EYE HOSPITAL.—5 p.m., Mr. T. M. Tyrrell: Management of Glaucoma.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Theatre, 5 p.m., Dr. G. B. Mitchell-Heggs: Common Skin Disorders of the Vulva.

SOCIETY OF APOTHECARIES OF LONDON.—4 p.m., Professor J. H. Dible: Pathology and the General Practitioner; 5.15 p.m., Dr. R. M. B. MacKenna: The Common Skin Diseases: Diagnosis and Treatment as Regards the General Practitioner.

WEST END HOSPITAL FOR NERVOUS DISEASES.—5.30 p.m., Dr. D. Gordon: When the Electroencephalogram Helps.

Wednesday, November 25

BIRMINGHAM MEDICAL INSTITUTE: SECTION OF PSYCHIATRY.—8 p.m., Presidential Address by Dr. J. J. O'Reilly: Criminal Responsibilities.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Cellular Naevi and Melanomata.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 9.45 a.m., Miss A. Bloomfield: Pruritus Vulvae.

INSTITUTE OF ORTHOPAEDICS.—8 p.m., clinical conference. Papers by Dr. Angus Macpherson, Mr. A. W. L. Kessel, and Mr. G. L. W. Bonney: Vascular Disturbances in Poliomyelitis.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. Harland Rees: Differential Diagnosis of Frequency of Micturition.

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Royal Free Hospital School of Medicine, 8.30 p.m., Mr. C. P. Wilson: Vasomotor Catarrh.

NORTH-WESTERN TUBERCULOSIS SOCIETY.—At Aintree Hospital, Liverpool, 5.30 p.m., Mr H. Morriston Davies: A Review of the Treatment of Pulmonary Tuberculosis and the Future Prospects.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Professor C. Rimington: Porphyrin Metabolism.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. H. S. Le Marquand: Obesity in Children (illustrated).
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE: EDINBURGH BRANCH.—At West Medical Theatre, Edinburgh Royal Infirmary, 5 p.m., Dr. B. A. Sybil Russell: Malaria as it Affects the Young in an Endemic Area.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Theatre, 5 p.m., lecture-demonstration by Dr. R. C. MacKeith: Psychological Medicine.

Thursday, November 26

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. H. E. Sigerist (Yale, U.S.A.): Science and History.
GLASGOW UNIVERSITY MEDICO-CHIRURGICAL SOCIETY.—At Glasgow University Union, 7.30 p.m., Dr. H. E. Hutchison: Any Old Iron?
HONYMAN GILLESPIE LECTURE.—At University New Buildings, Edinburgh, 5 p.m., Professor D. M. Douglas and Professor I. G. W. Hill: Some Aspects of Mitral Disease in Relation to Surgical Treatment.
●INSTITUTE OF CHILD HEALTH AND INSTITUTE OF NEUROLOGY.—At National Hospital, Queen Square, W.C., 5.30 p.m., Dr. M. Kremer: Sensory Defects in Paralytic Syndromes.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Tinea Infections.
LIVERPOOL MEDICAL INSTITUTION.—8 p.m., Dr. F. P. Hudson and Mr. P. P. Rickham: Emergencies in Newborn Infants; With Special Reference to Early Diagnosis and Management Outside Hospital.
LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Medical Society of London, 8.30 p.m., Sir John Parkinson: Syncope.
OXFORD UNIVERSITY.—At Nuffield Orthopaedic Centre, Wingfield-Morris Orthopaedic Hospital, 8.30 p.m., Mr. N. Capener: Evolution of Lateral Rachotomy.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Mr. J. Laver: Meaning of Military Uniforms.
ST. ANDREWS UNIVERSITY.—At Physiology Department, Dundee, 5 p.m., Mr. R. S. Handley: Carcinoma of the Breast.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. Desmond Curran: psychiatry demonstration.
SURREY INTER-HOSPITAL PSYCHIATRIC ASSOCIATION.—At Netherne Hospital, Coulsdon, Surrey, 7.30 p.m., Dr. A. A. Baker: Effects of Largactil in the Treatment of Psychotic Excitement; Dr. J. P. S. Robertson: Symmetry of Constructed Patterns; An Experiment with Psychotics; Dr. Sybille L. Yates: Problems in the Treatment of Neuroses in a Psychiatric Hospital; Dr. R. K. Freudenberg: Planning Aftercare for the "Long-stay" Psychiatric Patient.

Friday, November 27

INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. I. Muende.
MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES.—7.30 p.m., general discussion to be opened by Dr. R. R. Willcox and Mr. A. J. King: For and Against Treatment Before Diagnosis.
●POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. K. Shirley Smith: Clinical Features and Treatment of Shock in Cardiac Infarction.
●ROYAL INSTITUTION OF GREAT BRITAIN.—9 p.m., Sir Alexander Fleming, F.R.S.: Antibiotics.
ROYAL MEDICAL SOCIETY, Edinburgh.—8 p.m., Dr. Henry Yellowlees: The Psychiatric Situation.
ROYAL SANITARY INSTITUTE.—At Town Hall, Dudley, 10.15 a.m., Mr. W. Parker: Post-war Housing Trends; Dr. H. Paul: Infectious Disease—The New Look.
●SOCIETY OF CHEMICAL INDUSTRY: FINE CHEMICALS GROUP.—At London School of Hygiene and Tropical Medicine, 7 p.m., Mr. A. L. Bacharach: Writing Wrongs.

Saturday, November 28

INSTITUTE OF ORTHOPAEDICS.—10 a.m., clinical demonstration.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Crawford.—On October 7, 1953, at St. Mary's Hospital, Portsmouth, to Jeanne (formerly White), wife of Surgeon Lieutenant I. B. Crawford, R.N., a daughter—Belinda Jane.
Leaming.—On October 22, 1953, to Barbara, wife of Dr. Harry Leslie Leaming, D.A., a daughter—Isobel Joan.
Macdonald.—On November 12, 1953, at Cuckfield Hospital, Sussex, to Rose Ann (formerly Davies), wife of Duncan Donald Macdonald, M.B., B.Ch., a son—Malcolm Robin Howard.
Meldrum.—On November 2, 1953, at Stoneacre, Swinton, Manchester, to Betty (formerly Dunsmore), M.B.E., wife of Robert Meldrum, M.B., Ch.B., a daughter.

MARRIAGES

Spencer—Crane.—On October 27, 1953, at the Baptist Chapel and Consulate, Leopoldville, Belgian Congo, Michael Charles Spencer, B.M., B.Ch., to Philippa Joan Eldred Crane.

DEATHS

Alexander.—On October 29, 1953, Frederick Hugh Alexander, M.B., of Elmhurst, Angmering, Sussex.
Avery.—On October 30, 1953, at The Gables, Church Street, Ewell, Surrey, Leonard Avery Avery, D.S.O., T.D., M.R.C.S., L.R.C.P., Major, R.A.M.C., retired
Boger.—On October 29, 1953, at the Hospital of St. John and St. Elizabeth, St. John's Wood, London, N.W., Hugo Boger, M.R.C.S., L.R.C.P., of 43, Lauderdale Mansions, Maida Vale, London, W.
Crawford.—On November 2, 1953, Gilbert Stewart Crawford, C.M.G., M.D., D.P.H., D.T.M., Lieutenant-Colonel, R.A.M.C., retired, of 54, Victoria Road, Exmouth, Devon, aged 85.
Maybury.—On November 15, 1953, at St. Thomas's Hospital, Hydestyle, Surrey, Bernard Constable Maybury, M.B., F.R.C.S., of Weston Corbett House, Basingstoke, Hants, aged 65.
Maynard.—On October 20, 1953, John Seymour Maynard, M.D., of 16, Prince Edward Mansions, Pembridge Square, London, W.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Full-cream or Half-cream Milk?

Q.—*Is it best to prescribe full-cream national dried milk as the standard diet for all artificially fed babies, or should they be fed on half-cream for a period? Food officers seem reluctant to permit the half-cream and it is always much more difficult to get.*

A.—Very large numbers of normal, healthy babies are brought up from the beginning on full-cream cow's milk, whether fresh, evaporated, or dried. Similar numbers of equally healthy babies are brought up for the first few weeks on a half-cream dried milk. The idea behind the use of partially skimmed milk is that the fat of cow's milk is difficult to digest. This is said particularly to be the case with premature infants and those recovering from gastro-enteritis, and there seem to be occasional otherwise normal infants who do better on a half-cream (partially skimmed) milk.

The idea is disappearing that variations in the type of milk, and minute alterations in the proportions of fat, sugar, and protein, are important in the artificial feeding of the normal child. However, many mothers and many of the nursing profession still firmly hold this belief, and it is wise to use the type and brand of milk which the mother, grandmother, or nurse prefers, should she have a definite opinion.

Poliomyelitis at School

Q.—*A case of poliomyelitis has occurred at a boarding school, and parents have been given the option of taking their children home. What action is advised?*

A.—An answer to this query cannot be given without quoting the arguments for and against school closure.

There is no rule that can be applied as a generality in such a case. For example, a decision may be influenced by the circumstances of the single case, particularly if "imported." In that event it might be argued that the child, having contracted the disease before the opening of the term, had not necessarily spread the disease throughout the school. If he had one could merely await developments, as (apart from gamma globulin therapy, as yet impracticable here) nothing would be gained by breaking up the school; in fact, such a step could possibly disseminate infection to other areas. In the meantime, pending the completion of quarantine, steps should be taken to minimize the risk of dissemination of the virus by avoiding overcrowding and undue physical exertion and by maintaining close medical supervision.

If the case occurred more than three weeks after school opening, it could be reasonably inferred that the virus might be already widespread in the school. Here again procedure should differ little from that already described, except that there should be an intensification of separation and of medical observation of contacts, particularly those in closest contact.

In the event of a number of cases occurring, especially in successive generations, there would be a reasonable argument for closure. By that time, however, there might already be a widespread dissemination of virus without clinical disease, but with natural immunization occurring. However, the objections to closure already stated could be applied. It might be wise to advise apprehensive parents

to have their children home, provided they can ensure reasonable separation. The thinning of the ranks of the school might have a beneficial effect in checking virus spread.

Iron for Anaemia

Q.—*Does it matter whether iron tonics are taken before or after meals? Is it advisable to give acid with iron, and, if so, is glutamic acid any better for this purpose than hydrochloric acid?*

A.—Iron tonics have no place in rational therapy unless there is clear evidence of an iron-deficiency anaemia. Correct diagnosis usually requires a full haematological investigation. When treatment with iron is thus indicated, it is preferable to use preparations of ferrous iron, and these should be given after meals to avoid or reduce the side-effects of nausea and other gastro-intestinal disturbance due to the irritant action of these substances. There is no evidence that the taking of acid with the iron preparation increases the rate of regeneration of haemoglobin, the average daily increase to be expected from adequate amounts of iron being of the order of 1%.

The two most suitable oral preparations of iron are tablets of ferrous sulphate (3 gr.—0.2 g.) or iron and ammonium citrate (30 gr.—2 g.) in a fluid mixture, given thrice daily after food.

A Milli-equivalent

Q.—*What exactly is a milli-equivalent? What advantages has it as a unit for use in biochemical work?*

A.—A milli-equivalent (mEq) is that amount of a substance which is capable of reacting with or releasing, directly or indirectly, 8 mg. of oxygen. In water 2 atoms of hydrogen are combined with 1 atom of oxygen of atomic weight 16. Therefore 1 atom of hydrogen (1.008 g.) is equivalent to 8 g. of oxygen; 1 atom of hydrogen is 1 "equivalent," and 1 "milli-equivalent" (1.008 mg.) equates with 8 mg. of oxygen. In hydrochloric acid 1 atom of hydrogen is combined with 1 atom of chlorine, and therefore 1 milli-equivalent of chlorine (or chloride) is that number of milligrammes represented by its atomic weight—that is, 35.5 mg. An atom of chlorine is combined with an atom of sodium in sodium chloride, and a milli-equivalent of sodium is therefore 23 mg., while a milli-equivalent of sodium chloride is 23 + 35.5 = 58.5 mg. Similarly, in sodium bicarbonate ($NaHCO_3$) the milli-equivalent of carbon dioxide in the bicarbonate ion, HCO_3^-, is 44 mg. or 22.4 milli-litres of the gas CO_2 at standard temperature and pressure. For other substances one can calculate the amounts which react, in one way or another, with 1 milli-atomic weight of hydrogen (1.008 mg.) or half a milli-atomic weight of oxygen—that is, 8 mg.

In chemical reactions involving neutralization between acids and bases, and in oxidations and reductions, it is particularly convenient to think of the reactants in terms of equivalents or milli-equivalents. Thus in studies of acid-base balance it may be an advantage to express concentrations of plasma constituents which act as acids or bases in terms of equivalents, so that the "total acid" of the plasma may be compared with the "total base." In this way it can be seen if the concentrations of basic and acidic constituents add up to "balance," or if there is a preponderance of acid over base or *vice versa*—that is, whether the acid-base balance favours an acid or an alkaline state. Concentrations of the acid radicles (chloride, carbon dioxide (bicarbonate), phosphate, sulphate, proteins, and organic acids), and of the basic (sodium, potassium, calcium, magnesium) are therefore calculated as milli-equivalents per litre of plasma; the equivalent, that is, of the amount of acid or base which they represent or are capable of neutralizing. With simple monovalent ions like sodium and chloride the mg. per litre are divided by the atomic weight; with divalent ions—for example, calcium—by half the atomic weight. With plasma proteins, which act as weak acids and neutralize a certain quantity of base, one can express their concentration, as one would for an acid, in terms of the amount of the base they neutralize. The concentration of protein (in mg. per litre) is divided by the average equivalent weight of the plasma proteins—that is, by that fraction of their molecular weight which represents the amount which would neutralize one milli-equivalent of sodium hydroxide—that is, 1 litre of $N/1{,}000$ NaOH. For this purpose a factor is used—that is, g. protein (per 100 ml.) × 2.43 = milli-equivalents per litre.

Chemotherapy of Primary Tuberculosis

Q.—*What is the prevalent opinion on the chemotherapy of primary tuberculosis in children? This question is from India.*

A.—The general opinion in Britain is that chemotherapy has little effect on primary tuberculosis in children. This is probably because the main manifestation of primary tuberculosis in children is hilar glandular enlargement, and on this chemotherapy appears to have little effect. In the unusual cases where there is progression of the pulmonary component of the complex chemotherapy will be effective. Although, as mentioned, most authorities agree that chemotherapy has no dramatic effect in most cases of primary tuberculosis, it is not excluded that there might be some effect. In particular, the effect on the incidence of serious complications, such as miliary tuberculosis or tuberculous meningitis, or on later relapse of the tuberculosis, has not been seriously studied. It may be that the relative lack of effectiveness of chemotherapy in children of European race may not be paralleled in other races. A limited personal experience with young adult Indians with hilar glands enlarged as a result of a primary tuberculous infection suggests that these cases may respond well, and even dramatically, to chemotherapy.

Inheritance of Multiple Neurofibromatosis

Q.—*How is multiple neurofibromatosis (von Recklinghausen's disease) inherited?*

A.—Von Recklinghausen's disease is usually ascribed to a dominant gene, and this appears to be true of the bulk of the published cases. Fertility is considerably reduced, however, and in view of the incidence of the condition in the population the frequency of mutation is probably high. Skipping of generations also seems to occur commonly. This may sometimes be because there is much variability in severity, and slightly affected persons may be overlooked; it is also likely that the gene may not manifest itself at all on occasion. It is possible, though not proved, that in a small proportion of instances a recessive gene is responsible.

Correction.—In an answer to a question on "Stress and Arterial Disease" (*Journal*, November 7, page 1057) there appeared a statement on the attitude of the Ministry of Pensions and National Insurance. The Ministry writes: "This statement could be misleading. As a result of experience, it is not the general policy of the Department to admit aggravation of hypertension."

"Any Questions?" Book.—The second book of selected "Any Questions?" is available, price 7s. 6d. (postage 6d.). Copies may be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers.

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